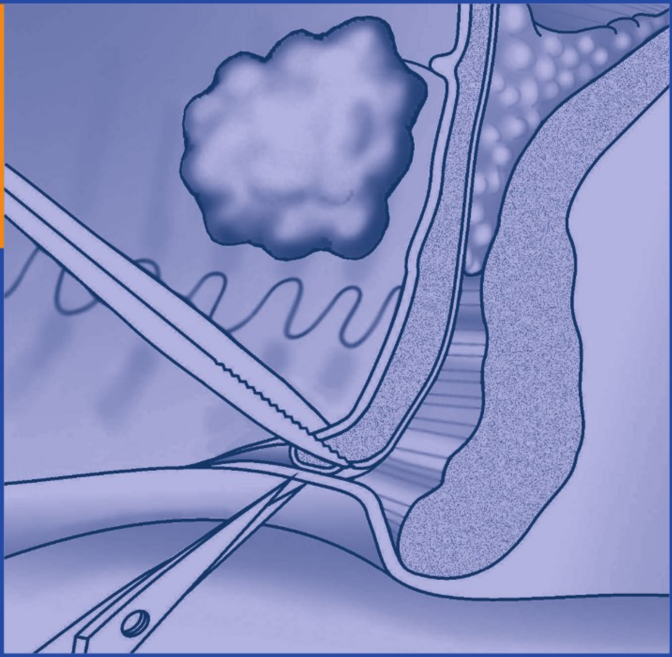
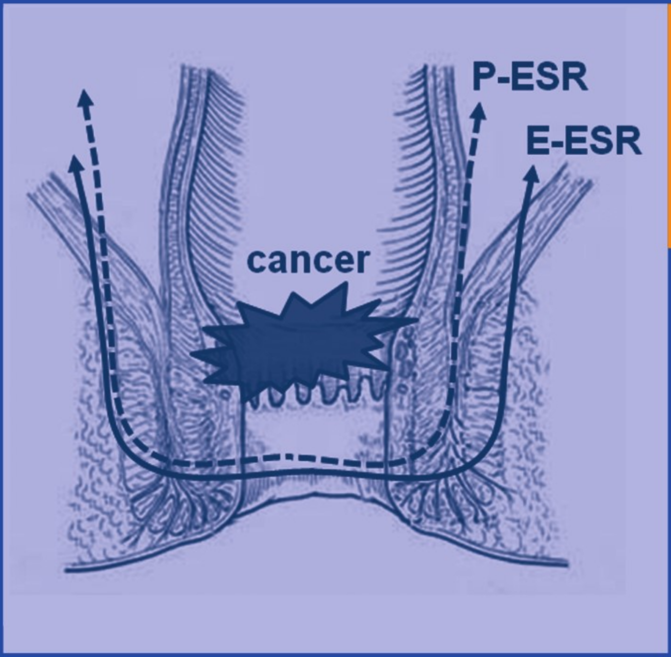
Rudolf Schiessel · Peter Metzger
Editors

Intersphincteric Resection for Low Rectal Tumors





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Intersphincteric Resection for Low Rectal Tumors

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Preface

Patients with rectal cancer expect from their doctors cure from the disease. Another goal is to keep the integrity of their body intact. Very often the first question of a patient will be: "Do I need a stoma?" We know that most people are worried by the announcement that a permanent stoma might be inevitable. The acceptance of a permanent stoma is higher in northern than in southern Europe, low in islamic countries and in eastern Asia.

The responsibility of the surgeon is to meet two goals: 1. To cure the cancer and 2. To save sphincter function. The development of rectal surgery has shown that in the early days the surgeons developed methods to avoid laparotomy because survival of the operation was the dominating goal. Later more radical procedures took place and for a long time abdominoperineal resection became the standard procedure. The growing knowledge about the lymphatic spread of rectal cancer and the further development of the surgical techniques opened the field for sphincter saving surgery. But anterior resection of rectal cancers was mainly applied to tumors of the upper third of the rectum. The reason was an overestimation of the longitudinal spread of rectal tumors. A distal resection margin with a minimum of 3 cm or more was the rule. This precluded many cases in the middle and lower rectum from sphincter salvage. A meticulous analysis of cases with different distal margins showed that margins up to 1 cm do not increase local recurrence. Therefore sphincter saving surgery could be extended to the middle third of the rectum. The development of circular stapling instruments enabled low rectal anastomoses. But even with low anterior resection patients with tumors of the lower third of the rectum, not invading the sphincter apparatus are very often treated by abdominoperineal resection, thereby sacrifizing a healthy sphincter apparatus. This is done in the fear of an unradical tumor resection and because of the technical difficulties which are common in the lower rectum especially in obese males. The authors of this book will share their experience with you in the treatment of tumors of the lower rectum applying latest advances in diagnostic and therapeutic measures.

With a coded link you can watch videos showing the technique of:

1. *R. Schiessel: Intersphincteric resection for low rectal tumors: The open technique*
2. *P. Metzger, M. Hoffmann, R. Schiessel: Laparoscopic technique of intersphincteric resection for low rectal tumors*
3. *Seon-Hahn Kim: Robot assisted intersphincteric resection*

We are proud, that so many international experts have agreed to contribute to this book and we hope that this book will help our surgical colleagues in their decisions.

Rudolf Schiessel
Peter Metzger

Contents

Pathology of low rectal cancer

The pathological assessment of the surgical specimens originating from the lower rectum and anal canal

Barna Bogner

Development and anatomy of the anorectal wall and surrounding structures

The most profound investigation of the anorectal development was performed by Aigner et al. on 79 fetuses from the ninth week on postconceptionem [1]. According to their results during the early prenatal life, the muscular layers of the rectum and of the anal canal derive from the mesenchyme that accompanies the endodermal part of the anorectum. The inner circular layer of the rectum precedes the outer longitudinal layer during the seventh week of embryonic development. The anlagen of the levator muscle and the external sphincter occur within the surrounding mesenchymae. They are clearly separated from each other and they both show the signs of proliferative activity when they get in contact with the bundles of the smooth muscles deriving from the outer longitudinal layer of the rectal wall. As a result both the levator ani and the external sphincter grow larger and get in contact (Fig. 1).

The levator ani muscle is continuous with the deep portion of the external anal sphincter muscle. At the level with the puborectalis portion of the levator ani muscle, the rectal adventitia constitutes a thin, microscopic layer that is interposed between the outer longitudinal muscular layer and the inner fascia of the levator ani muscle. This is an important finding as there is a contradiction of the intepretation of this region in the anatomical textbooks which has an effect on staging and therapeutical procedures. The schematic drawing in the AJCC Cancer Staging Atlas depicts a situation where the levator ani muscle is attached to the muscular layer of the rectum over the external sphincter [2]. As a result the invasion of the external sphincter is classified as a T3 tumor, whereas the involvement of the levator muscle means T4, which is contradictory as both muscular structures are primarily of mesodermal origin [1]. All the other anatomical sources show a different situation, where the puborectalis part of the levator ani muscle is continuous with the external levator muscle [3–5]. The wall of the anal canal is composed of the anal canal mucosa, submucosa, and muscularis, which is composed of the thick inner circular layer, serving as the internal sphincter whereas the outer longitudinal layer continues with a small layer of connective tissue which separates the longitudinal layer from the striated external sphincter. The inner circular layer is a continuation of the circular muscle coat of the rectum but is considerably thicker. Its thickness varies depending upon the height, the mode of investigation and among investigators – according to Sternberg, in histological sections it measures 5 to 8 mm and ends 5 to 19 mm below the dentate line [3], whereas it is only 1.5 to 3.5 mm thick according to the Gray's Anatomy. The opinions vary on the anatomy of the longitudinal muscle as well. According to Shafik it consits of three layers, whereas others regard it as a conjoint coat [3, 4]. At the lower end of the internal sphincter it breaks up into a number of septae, which diverge fanwise through the subcutaneous part of the external sphincter. There is no complete agreement either over the number of muscle fibers of the lower part of longitudinal muscle, or over its composition. According to Morgan and Thompson, the fibers become more fibroelastic [5] or completely fibro-elastic [4] as they pass through the external sphincter. Macchi et al. investigated 8 male and 8 female cadavers (age range 52–72 years) with special stains for elastic fibers and using monoclonal antihuman alpha-smooth muscle actin and monoclonal anti-rabbit sarcomeric actin and monoclonal anti-rabbit sacromeric actin. Although they agree that the proximal attachment of the longitudinal anal muscle (LAM) is in continuity with the longitudinal muscle of the rectum, immunohistochemically the muscle showed predominantly striated muscle fibers, with a few smooth muscle fibers. On coronal sections they were able to identify the LAM only in 83% of their specimens, *where the LAM received fibers from the puborectalis muscle and terminated in 7–9 fibro-elastic septa which penetrated the external anal sphincter [6].* The histological composition

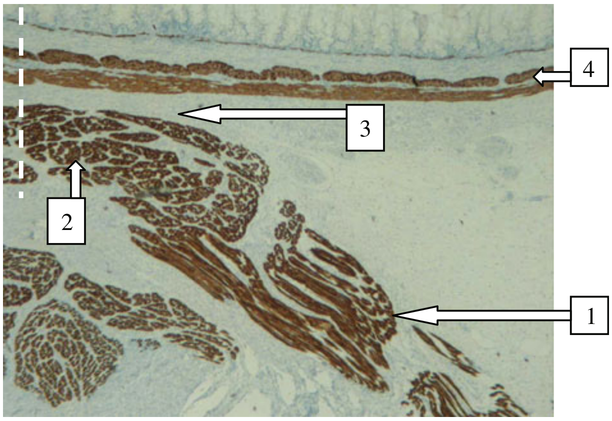

Fig. 1. The continuity of the levator ani (1) and external sphincter muscles (2). This functional and anatomical unit is clearly separated by the intersphincteric space (3) from the external longitudinal and inner circular layers of the rectal wall (4). (Desmin ×40) According to the dashed line the corresponding structures can be visible on the horizontal plane on the Fig. 4

of the LAM is important from the functional point of view after intersphincteric resection. Its lower region can show individual developmental differences and can change its histological characteristics with the advancing age. We investigated the longitudinal sections of three fetal pelves from 20, 22 and 35 weeks postconception with hematoxylin-eosin stain and smooth muscle actin and desmin immunohistochemistry (Fig. 2).

In the first case (Fig. 2A) the LAM's lower fibres are intermingled with the fibers of the external anal sphincter (EAS), in the second specimen (22 p.c.) (Fig. 2B) the LAM is terminated above the external sphincter (arrow), whereas in the third case (35 weeks p.c.) a mixed pattern could be visible. The spaces between the striated muscle fibers of the EAS were filled with connective tissue (Fig. 2B, D) which is devoid of elastic fibres. Shafik et al. gain a similar finding in dogs, where only 70% of the EAS showed smooth muscle fibres scattered between

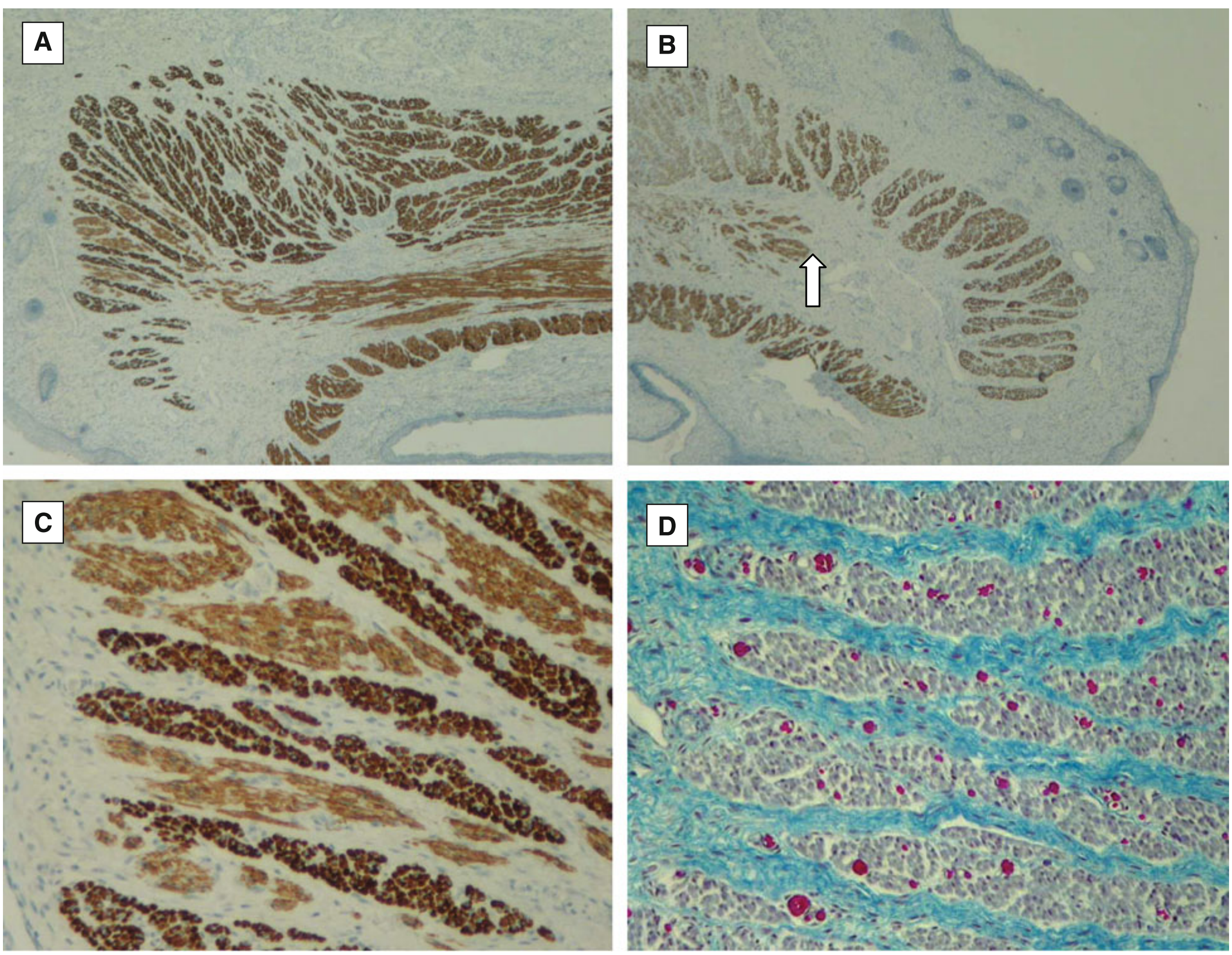

Fig. 2. **A** Fetal sphincter complex 20 weeks postconception. **B** 22 weeks postconception. The desmin stain resulted in a homogenous light brown shade in the smooth muscle fibres as this intermediate filament attaches to the dense bodies which are distributed throughout the sarcoplasm of the smooth muscle cell. The desmin forms a lattice that surrounds the sarcomere at the level of the Z lines, resulting in a dark brown staining [7] (**A**, **B** – Desmin 20X, **C** – Desmin 100x, **D** – Mallory's trichrom 100x)

the striated fibres. These smooth muscle fibres can be responsible for the resting tone of EAS. After internal sphincter resection they found characteristic changes in the EAS, namely degenerative and hypertophic changes after 2nd to 5th month, regeneration of the striated muscle from 6th to 10th month and an increase in the number of smooth muscle fibres which resulted in a “compound” muscle [8]. We hypothesize that in those patients in whom the LAM terminates over the EAS, the regenerative capacity can be lower and it can influence the functional outcome after ISR.

The pathological investigation and staging of the lower rectal/anal canal cancers

The dissection and reporting of the surgical resection specimens from this area should be performed according to the international guidelines. The Guideline of the Royal College of Pathologists in the United Kingdom gained widespread acceptance [9]. The macroscopic examination of the specimen is critical and of a prognostic significance. The anterior and posterior surfaces should be photographed to record any perforation and the plane of surgical dissection. The specimen is opened anteriorly till the level of peritoneal reflection and filled with some absorbent material to reach the best possible fixation which is important for the following immunohistochemical and molecular investigations. The non-peritonealized (circumferential) surgical margins are painted with ink. The specimen should be fixed for 48 h or longer and the whole specimen should be sliced at 3–5 mm interval. These slices should be photograped again to document the plane of surgical dissection. Unfortunately, the Guideline of the Royal College of Pathologists for Reporting Colorectal Cancer Specimens [9] does not contain information about the anal canal area. In this aspect the College of American

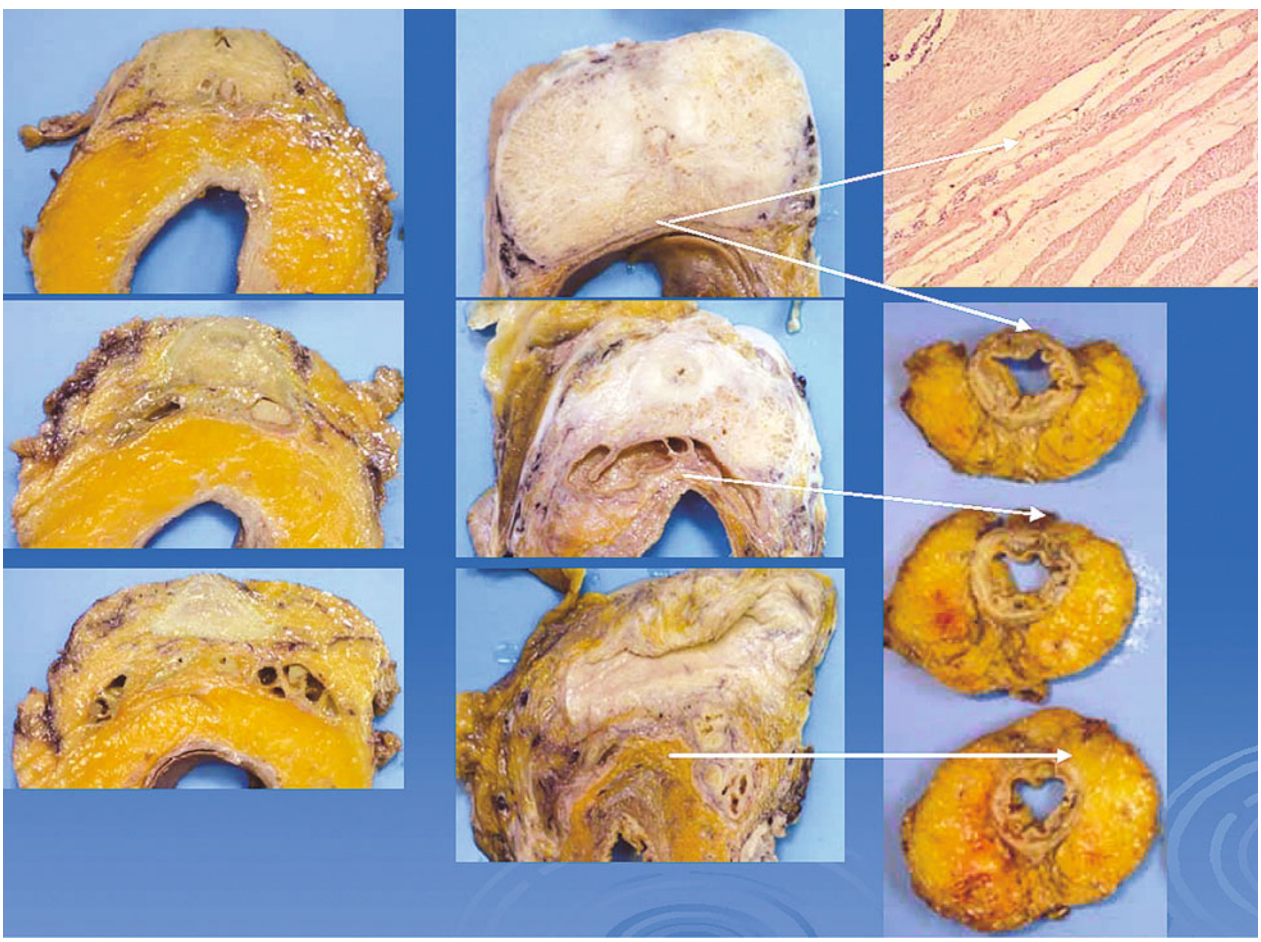

Fig. 3. Comparison of a two male cadaveric specimen with a surgical specimen after TME. There is good bulk of mesorectum anteriorly on the left and complete absence at the level of the prostate on the right specimen. The histological insert shows the absence of fat cells and the close proximity of the prostate to the rectal wall. The plane of excision in the TME specimen is the mesorectal fascial plane

Pathologists Protocol for the Examination of Specimens from Patients with Carcinoma of the Anus can be used [10]. Although the surgical planes of dissection in the mesorectal area are well defined, i.e. the mesorectal fascial, intramesorectal and muscularis propria plane, they are not clear enough after intersphincteric resection.

The definitions of the surgical planes after TME [9, 11]

Mesorectal fascial plane/Complete

The mesorectal surface is smooth with only minor irregularities of its surface such that no defect is deeper than 5 mm. The mesorectum itself is of *good bulk anteriorly* and posteriorly and there is no 'coning' near the tumour.

Intramesorectal plane/Nearly Complete

The mesorectum is of moderate bulk but the mesorectal surface is irregular. *The muscularis propria of the rectal wall is not visible except at the area of insertion of the levator muscles*. Moderate coning of the specimen is present distally.

Muscularis propria plane/Incomplete

There is little bulk to the mesorectum and its surface is irregular with deep cuts and tears, some of which extend on to a visible muscularis propria.

We find these definitions are problematic in two aspects: 1. The thickness of the mesorectum anteriorly is far from "*good bulk*" (Fig. 3). Our yet unpublished investigation on 52 male cadavers in this area showed a great variation in this mesorectal thickness. According to the non-parametric Spearman correlation test the thickness of abdominal fat and the anterior mesorectum showed linear correlation ($p < 0{,}0001$) at the level of seminal vesicle –rectum and the bladder- ductus deference -rectum.

Our results are in keeping with the morphometric assessment with magnetic resonance imaging of the mesorectum performed by Torkzad et al. and prove the steep decrease of mesorectal thickness (tapering of the mesorectum) in the lower prostatic region (Table 1).

Table 1: The thickness of the mesorectum anteriorly in mm

Level	Min (mm)	Max (mm)	Average (mm)
Bladder	0	25	3,94
Middle prostatic	0	17	3,03
Lower prostatic	0	13	0,34
Torkzad and Blomqvist [12]	0	28	3,03

2. *At no site is the muscularis propria visible with the exception of the area of insertion of levator muscles.* As we presented beforehand the muscularis propria can be visible at the lower-anterior part of the rectal resection specimens in the male patients, moreover it is clear from the anatomical considerations that the levator muscle is not inserted to the rectal wall as it continues in the external anal sphincter. Consequently, under the level of the termination of the mesorectum the muscular wall must be visible which cannot be equalled with the poor surgical quality. On the contrary, the intersphincteric resection which is a procedure conducted in the intersphincteric plane with the resection of the internal sphincteric muscle will produce a "voluntary muscularis propria plane".

We can draw the conclusion, that the pathologists ideally have to be in close cooperation with the surgeons and the radiologists to get familiar with the nature of surgical procedure and the thickness of the mesorectum at different levels before the cutup and macroscopic assessment of the surgical planes.

The rate of circumferential margin (CRM) involvement/R status

The main goals of surgery in case of lower rectal/anal canal cancers are the free circumferential margin to avoid the local recurrence on the one hand and retaining the continence on the other. This can be achieved with a precise preoperative imaging, the use of neoadjuvant chemoradiation in advanced cases and a good surgical quality. The rate of CRM involvement depends on the stage of disease, the quality of surgery, the efficacy of properative neoadjuvant chemoradiotherapy (CRT), the timing of surgery after CRT, the definition of CRM involvement and the quality of pathological reporting. Kuo et al. reported a 13.3% CRM involvement which is relatively high compared with others (Schiessel et al. 3%, Portier et al. 4%, Chamlou et al. 4.4%) but 88.5% of their patients had locally advanced cancer and received preoperative chemoradiation [13]. Although there is a consensus about the definition of CRM involvement, i.e. the distance of tumor and surgical margin is $\leq$1 mm or the margin is directly invaded by the tumor (R1dir) [9, 15], there are still publications in which the margin involvement is defined as $\leq$2 mm [13, 14]. It would be important to know whether like in the adenocarcinoma of the esophagus the R1dir and the R1$\leq$1 mm group are prognostically different, as the very close vicinity of vital organs of the mediastinum in the case of esophageal resection and the proximity of the external sphincter in ISR creates a similarly difficult surgical situation [16].

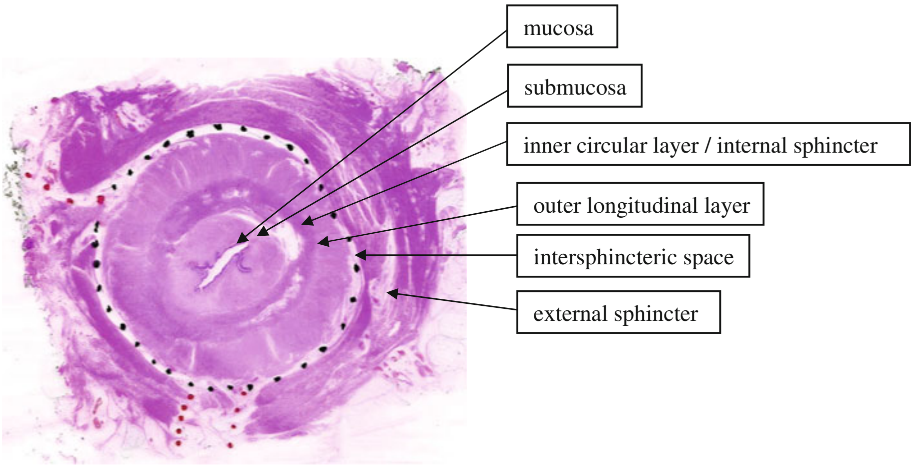

Fig. 4. Large histological section (macroblock, HE) from the anal canal. A loose connective tissue fills in the intersphincteris space (black dots). The external sphincter is discontinuous at two sites (red dots)

The usefulness of large histological sections

As I have mentioned, the CRM involvement is dependent on the pathological reporting. Its investigation can be performed via multiple sections, in which the direct extension of the primary tumor, a metastatic lymph node, vascular or perineuralar invasion or a satellite peritumoral nodule is close to the inked margin. Although it is technically demanding, the use of large histological sections (Fig. 4) has many advantages:

- the assessment of CRM involvement is easier
- it is the best way to find the microscopic foci of residual cancer after neoadjuvant chemoradiotherapy (CRT)
- it helps to characterize the CRT effect on the surrounding tissues i.e. nerves and parts of the external sphincter if resected
- the comparison of the large histological sections and the preoperative images have a great impact on the work of every multidisciplinary team member dealing with lower rectal-anal canal malignancies [17].

The TNM stage of the lower rectum/anal canal cancers

The determination of the site of origin in the carcinomas overlapping the anorectal junction can be problematic. Because of possible differences in staging and regional lymph node at risk of metastasis among cancers of the anal canal, the rectum and the perianal skin, it is decisive to assure that the anatomic site is the anal canal or the rectum. The documentation of the anatomic site often requires a clinical correlation [10]. For staging purposes, such tumors should be classified as rectal cancers if their epicenter is located more than 2 cm proximal to the dentate line and as anal canal cancers if their epicenter is 2 cm or less from the dentate line [19]. The examination of the dentate line is easy in an opened resection specimen, but the pathologists are obliged to fix the specimens in unopened fashion and must find it after 3 to 5 mm serial sectioning [9]. The transition of the whitish squamous mucosa of the anal canal to the grayish-brownish colonic epithelium helps determine its position (Fig. 5).

A strongly disputed issue of the TNM classification is the satellite peritumoral nodule or tumor deposit, which is an invasive tumor focus in the mesorectum without the evidence of residual lymph node. It can represent discontinuous tumor spread, venous invasion with extravascular spread or a totally replaced lymph node. The TNM 5th, 6th and 7th edition repeatedly changed its definition

Fig. 5. The transition of squamous anal canal and colonic epithelium

which resulted in the refusal of the use of later classifications in many countries [18]. The introduction of the N1c category, i.e. tumor deposit/s in the subserosa or perirectal tissues without regional nodal metastasis is problematic in the case of anal canal tumors as there is no such category in this anatomical compartment, but the metastasis of perirectal lymph node/s means the N1 stage. It is not clear whether the N1c category of the rectum can be used as N1 stage in the anal canal tumors [19]. The version of TNM used should be stated in any pathological report and publications.

The risk factors for recurrence after intersphincteric resection

The long term results are dependent on many factors. Shirouzu et al found that the anus-preserving operation with sphincter muscle resection is not feasible for those tumors where the lowest edge is below the dentate line and where a preoperative biopsy shows a poorly differentiated or mucinous adenocarcinoma, even if the intermuscular groove is macroscopically unaffected by the tumor [20]. The measurment of the distance from the dentate line in low rectal tumours is also suggested by the Royal College of Pathologists as this can give an idea of the location of the tumor in relation to the internal sphincter [9]. The pathological stage (Dukes and p(y)TNM), positive microscopic resection margin, perineural invasion, lymphovascular invasion, poor differentiation, mucinous or signet ring cell histology, focal dedifferentiation (budding) are proved to have an effect on local recurrence or distant metastases [21–24].

The histological consequences of neoadjuvant chemoradiotherapy (CRT) in the anal complex

The goal of neoadjuvant radiotherapy is the downsizing and downstaging of the rectal and anal canal carcinomas before surgical intervention. In optimal case there is a minimal dose of radiation in the surrounding tissues, with a high dose administered to the target tumor volume. There is a constant debate about its role on the anal sphincter complex and the consecutive functional outcome. There might be a critical threshold amount of rectal tissue that can tolerate a radiation dose without complication, and that threshold can vary among patients. The compartments of the sphincter complex differ in their radiation susceptibility, i.e. the internal sphincter is more sensitive than the external one [25]. It should be noted that the functional outcome is dependent on many factors, the structures involved by the surgery, the quality of surgery, the age and anatomical variations of the patient (Fig. 2), the preoperative functional status, the mode and dose of irradiation and lastly the success of exclusion of the external sphincter from the field of radiation [25–27]. The role of pathologists is to interprete the histological effects of CRT in the surgical specimens after ISR. During this activity the pathologist should keep in mind that not only the staging and the regression grading are important, but also the histological characterization of radiation-induced damage in the sphincter muscles and myenteric nerves.

The quantification of fibrosis can be performed according to da Silva et al whose semiquantitative assessment for fibrous replacement is the following: Grade 0, up to 10 percent replacement; Grade I, 10 to 30 percent replacement; Grade II, 30 to 50 percent replacement; Grade III,

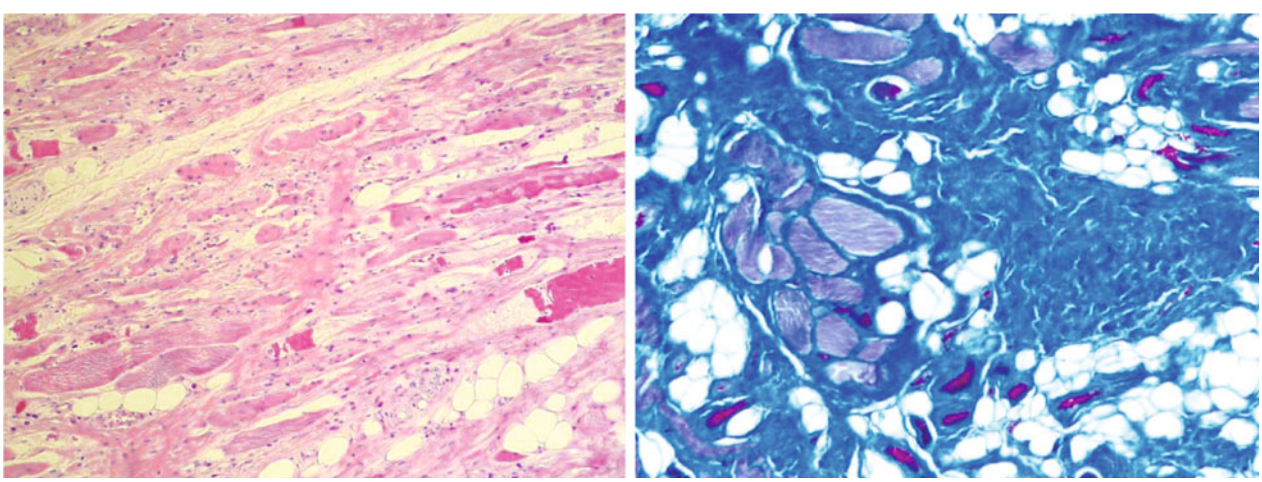

Fig. 6. External sphincter muscle after CRT. HE and Mallory’s trichrom stain 40×

> 50 percent replacement [25]. Although the number of patients enrolled in the investigation of this phenomenon is relatively small, their findings are similar – namely Grade II and III fibrosis were found in 75% vs 73% of the CRT treated patients, and Grade 0 and I in 67% vs 86% without CRT respectively [25, 28].

The post-CRT peripheral nerve degeneration can be characterized by density and hypertophy of the nerve bundles in the myenteric plexus and with cytological changes, i.e. the karyopyknosis, vacuolar degeneration, acidophilic degeneration of the cytoplasm, denucleation and adventitional neuronal changes [25, 28]. The nerve density is significantly increased after CRT [25]. It seems, that the postoperative anal dysfunction is not associated with each feature of neuronal degeneration. The post-operative anal dysfunction does not seem to be associated with each feature of neuronal degeneration, however there is a significant correlation with the total degeneration score [28]. Although the function can improve with the postoperative course suggesting that nerves and muscle can regenerate, it is fairly improbable in cases where the fibrosis and lipomatous metaplasia are as intense like as in Fig. 6. As a summary, the pathologists have to mirror the morphological outcome of CRT, in order to help increase the efficacy of the combined sphincter preserving treatment in their multidisciplinary team.

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Preoperative diagnostic procedures

Endorectal ultrasound for preoperative staging

Bryan Loh, Martin R. Weiser, and W. Douglas Wong†

Introduction

Evaluation of the anus and rectum has traditionally been done through external examination, digital rectal examination, anoscopy, flexible or rigid proctosigmoidoscopy, and colonoscopy. Imaging techniques have included barium enema, CT scan, and MRI. With the introduction of endoluminal ultrasonography, a greater degree of objectivity has been implemented in the evaluation of the anorectum. This is especially important in the evaluation and treatment of rectal cancer. Accurate preoperative staging guides decision for neoadjuvant therapy, sphincter sparing procedures, and local excision. Endorectal ultrasound (ERUS) and endoanal ultrasound (ERAS) are also used in the diagnosis of benign mucosal lesions, fistula in ano, fecal incontinence, anorectal abscesses, and extrarectal masses. This chapter will focus on the use of endoluminal ultrasound in the evaluation of low rectal cancer, with particular attention to decisions regarding intersphincteric resection of low rectal tumors.

Staging of rectal cancer

Historically, rectal cancer was staged using the Dukes classification developed by Sir Cuthbert Dukes [1]. The classification was based on depth of invasion of the bowel wall and regional lymph node metastases. Stage A was defined as tumor confined to the bowel wall, stage B as tumor extending through the bowel wall and stage C as tumor metastatic to regional lymph nodes. A later modification included stage D, which denotes distant metastasis.

In 1949, Kirklin et al. modified the Dukes classification to subdivide category B into B1 and B2, with depth of penetration to the muscularis propria as a reference [2]. Stage B1 was defined as penetration into, but not through, the muscularis propria. Stage B2 was defined by tumor penetration through the muscularis propria. Aster and Coller further refined the staging to C1, C2, and C3 to include node positivity [3].

The standard in the United States is the tumor, node, metastasis (TNM) staging system. Addition of the prefix "u" indicates staging that has been performed by ultrasound [4]. The American Joint Committee on Cancer (AJCC)-endorsed TNM staging for rectal cancer is shown below [5].

TNM staging system for rectal cancer [5]

Primary tumor (T)

Tx: No description of the tumor's extent is possible because of incomplete information.
Tis: The cancer is in the earliest stage (*in situ*). It invades only the mucosa.
T1: The cancer has grown through the muscularis mucosa and extends into the submucosa.
T2: The cancer has grown through the submucosa and extends into the muscularis propria.
T3: The cancer has grown through the muscularis propria and into the outermost layers of the colon and rectum but not through them. It has not yet reached any nearby organs or tissues.
T4a: The cancer has grown through the serosa.
T4b: The cancer has grown through the wall of the colon or rectum and is attached to or invades into nearby tissues or organs.

Regional lymph nodes (N)

Nx: No description of lymph node involvement is possible because of incomplete information.
N0: No cancer in nearby lymph nodes.
N1a: Cancer cells are found in 1 nearby lymph node.
N1b: Cancer cells are found in 2–3 nearby lymph nodes.
N1c: Small deposits of cancer cells are found in areas of fat near lymph nodes but not in the lymph nodes themselves.

N2a: Cancer cells are found in 4–6 nearby lymph nodes.
N2b: Cancer cells are found in 7 or more nearby lymph nodes.

Metastases (M)

M0: No distant spread is seen.
M1a: Cancer has spread to 1 distant organ or set of distant lymph nodes.
M1b: Cancer has spread to more than 1 distant organ or set of lymph nodes, or to distant parts of the peritoneum.

Stage grouping

Stage 0: Tis, N0, M0
Stage 1: T1-T2, N0, M0
Stage IIA: T3, N0, M0
Stage IIB: T4a, N0, M0
Stage IIC: T4b, N0, M0
Stage IIIA: T1-T2, N1, M0 or T1, N2a, M0
Stage IIIB: T3-T4a, N1, M0
T2-T3, N2a, M0
T1-T2, N2b, M0
Stage IIIC: T4a, N2a, M0
T3-T4a, N2b, M0
T4b, N1-N2, M0
Stage IVA: Any T, Any N, M1a
Stage IVB: Any T, Any N, M1b

To assist in clinical decision-making, the Colorectal Service at Memorial Sloan-Kettering Cancer Center (MSKCC) has proposed a modification of the ultrasound staging system. This is shown below.

MSKCC modified ERUS staging system

Stage			Treatment
uTw	uT0/T1	N0	Amenable to local excision
uTy	uT2/superficial uT3	N0	Recommend radical surgery
uTz	Deep uT3/any uT4	N0/N1	Recommend neoadjuvant therapy followed by radical resection
uN1	Probable or definite		Recommend neoadjuvant therapy
uN1	Equivocal		Base treatment on tumor stage and pathologic features

Equipment and technique

ERUS requires minimal patient preparation with two enemas prior to the examination. For examination, the patient is placed in the left lateral decubitus position. No sedation is required. An external examination and digital rectal examination are performed. Next, a handheld endocavitary probe with rotating transducer and 360 degree image is placed. At MSKCC, we use a Brüel and Kjær 2101 Hawk scanner (Naerum, Denmark) with a type 1850 rotating endosonic probe and a 10 MHz 6004 transducer. We also use a 2050 probe with capability for a 10, 12, or 16 MHz multifrequency transducer. The 10 MHz transducer with 1 to 4 cm focal length is commonly used, allowing for excellent visualization of perirectal tissues and image clarity. A 7.0 MHz transducer provides a focal length of 2 to 5 cm for deeper structure evaluation but has less resolution. The probe rotates 4–6 cycles per second and provides a 360-degree radial scan of the rectum and surrounding structures. It is important to keep the probe centered in the lumen. Scanning is done with the transducer directly in the rectum or, if difficult to pass, a proctoscope may be placed with the transducer and advanced proximal to the tumor. For the 1850 probe, the balloon is filled with 30 to 60 ml of fluid and passage of the probe is done from proximal to distal. Still frames of the ultrasound may be recorded at different levels of the rectum. The probe and attached proctoscope are withdrawn together, to assess the mesorectum for evidence of nodal metastases and depth of penetration. Upon reaching the levators, the balloon is desufflated and the probe withdrawn. The balloon is replaced with a fluid-filled, hard, translucent plastic cap. We use the Brüel and Kjær type UA0453 cap to continue the endoanal ultrasound.

Normal ERUS anatomy

The initial classification of rectal tumors was proposed by Hildebrandt and Feifel in 1985 [6]. In 1986, Beynon et al. proposed a five-layer model of the rectal wall based on anatomical studies and demonstrated that the layers seen in an ultrasound correspond directly to the anatomic layers present in the rectal wall [7] (Fig. 1). These five layers, from the center to the periphery, are as follows:

First hyperechoic layer: Interface between the balloon and the rectal mucosal surface
Second hypoechoic layer: Mucosa and muscularis mucosa
Third hyperechoic layer: Submucosa
Fourth hypoechoic later: Muscularis propria
Fifth hyperechoic layer: Interface between the muscularis propria and perirectal fat

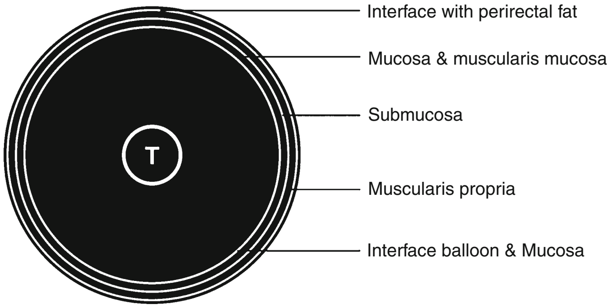

Fig. 1. Five-layer model of the rectal wall. The layers seen in a normal endorectal ultrasound correspond directly to the anatomic layers present in the rectal wall. "T" represents transducer

Assessment of rectal neoplasms

uT0 lesions

uT0 lesions are benign, noninvasive lesions confined to the mucosa. On ERUS imaging, the mucosa (inner black band) is expanded, with an intact submucosa (middle white hyperechoic line) (Fig. 2). Examples include benign rectal adenomas. uT0 lesions may be treated with local excision. ERUS should be performed prior to excision to completely evaluate the lesion, as it would be inappropriate to perform a submucosal dissection/local excision if there were a focal area of invasion identified within a villous adenoma. ERUS is reliable in distinguishing benign lesions, with reported accuracy ranging from 87% to 96% [8]. ERUS may detect malignant focus within a villous adenoma [9] that may not otherwise have been detected due to biopsy sampling error. In 2004, Worrell et al. published a metaanalysis of 258 biopsy-negative rectal adenomas from five studies. Focal carcinoma was detected in 24% of specimens on pathology. ERUS correctly established the diagnosis in 81% of these cases, decreasing the rate of misdiagnosis from 24% to 5%. Therefore, ERUS should be utilized routinely in the evaluation of rectal villous adenomas [10].

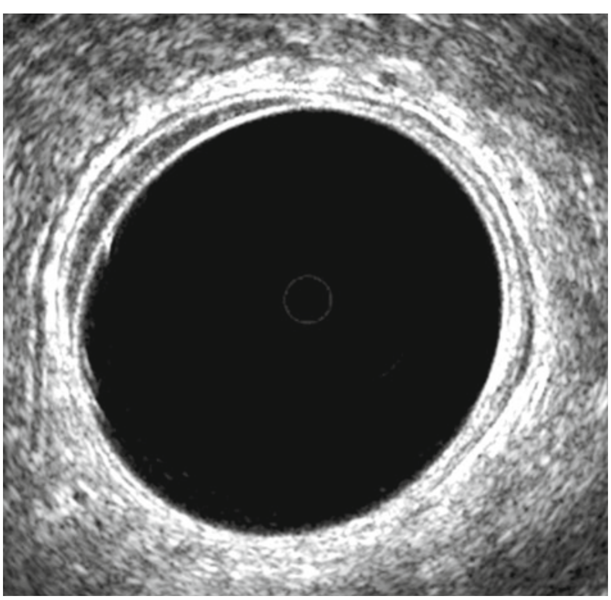

Fig. 2. uT0 lesion. A benign uT0 lesion can be seen in the right anterolateral aspect of rectum. The mucosa (inner black band) is expanded, with an intact submucosa (middle white, hyperechoic line)

uT1 lesions

uT1 lesions are early invasive cancers that infiltrate into the mucosa and submucosa without penetrating into the muscularis propria. uT1 lesions appear sonographically with irregular submucosa (middle white line) but do not invade the muscularis propria (outer black line) (Fig. 3). There may be a thickening or stippling of the submucosa without any break in the submucosal layer. A distinct break in the submucosa (middle white line) with invasion into the muscularis propria (outer black line) would constitute a T2 lesion. Local excision with either transanal excision (TAE) or transanal endoscopic microsurgery (TEM) is an acceptable treatment for select T1 lesions. Criteria for local therapy include tumor size less than 4 cm, involvement of less than one-third of the rectal circumference, well- to moderately-differentiated histology, absence of lymphatic or vascular invasion, and no involvement of the perirectal lymph nodes [11]. However, a 6–18% rate of nodal metastasis has been reported in the setting of T1 rectal cancer [12–14]. Accuracy in evaluating uT1 lesions ranges from 47% (in a study by Garcia Aguilar et al. in 2002) to 96% (in a metaanalysis by Kwok et al.) [8, 15]. In T1 adenocarcinomas, the accuracy of ERUS is lower because of occult metastasis, which may

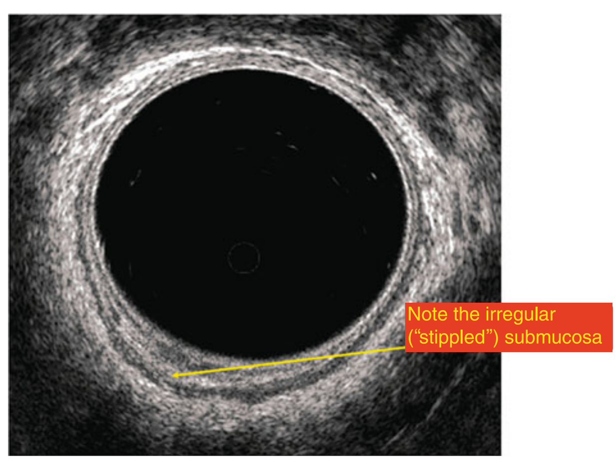

Fig. 3. uT1 lesion. A uT1 lesion is seen at the posterior aspect of the rectum. The submucosa (middle white line) is irregular, or "stippled", but does not invade the muscularis propria (outer black line)

be micrometastatic (< 1 mm) and thus cannot be visualized [16]. Similarly, Bentram in 2005 reported local recurrence rates of 15% for T1 adenocarcinomas following transanal excision, much higher than the rate of local recurrence following radical surgery [17]. Therefore, although select uT1 patients may undergo local resection, this should be done with caution as there are limitations in ERUS preoperative nodal staging and increased risks of local recurrence. At MSKCC, we generally recommend radical resection for good-risk patients with uT1 rectal cancer based on the higher rates of local recurrence following local excision vs. radical resection.

uT2 lesions

uT2 lesions penetrate into but not through the muscularis propria. Sonographically, this appears as a distinct disruption of the submucosa (middle white layer) (Figs. 4, 5). There is an expansion of the muscularis propria (outer black line) with the interface between the muscularis propria. The accuracy of ERUS in staging uT2 lesions is approximately 68% [8]. Nodal metastasis is reportedly as high as 17–47% [13, 18]. Radical surgery (either sphincter-sparing resection or abdominal perineal resection[APR]) for acceptable surgical candidates is recommended for uT2 lesions. Local therapy is reserved for high-risk surgical candidates with uT2 tumors, for patients requiring palliation, or for patients who require APR but refuse to have a permanent colostomy. Local recurrence rates of T2 tumors treated with local surgery alone is reportedly as high as 47%, with low survival rates of 65% [19–21]. Postoperative chemoradiation treatment should be considered after local therapy to reduce the risk of local recurrence [22]. Neoadjuvant chemoradiation in combination with local excision can also be considered for select uT2N0 rectal cancers. In a recent phase II clinical trial, a pathologic complete response (pCR) was demonstrated in 44% of patients who underwent neoadjuvant chemoradiation therapy followed by local excision. Overall, 64% of patients were downstaged to ypT0-1 [23].

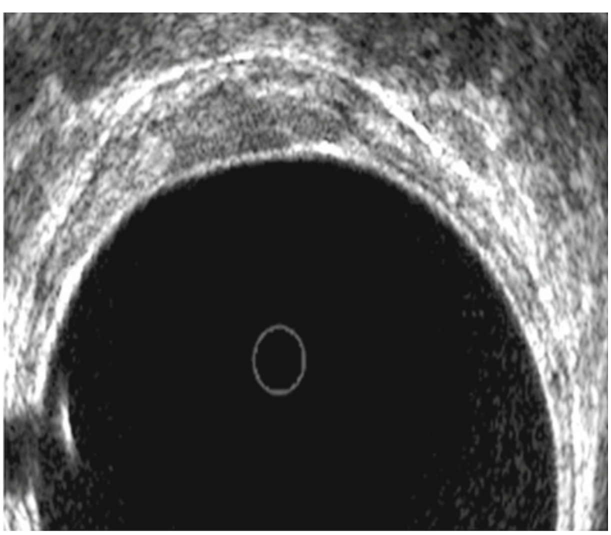

Fig. 4. uT2 lesion. An early uT2 lesion is seen in the anterior aspect of the rectum. There is distinct disruption of the submucosa (middle white layer), with expansion of the muscularis propria (outer black line)

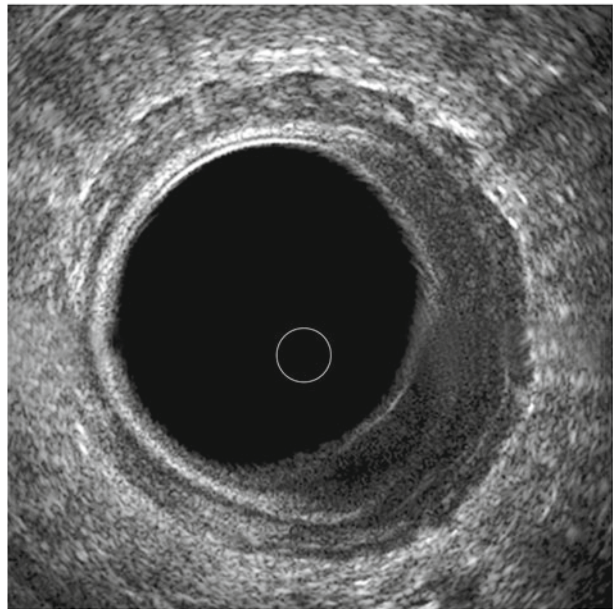

Fig. 5. Deep uT2 lesion. A deep uT2 lesion is seen in the left posterior lateral aspect of the rectum. Note the clear submucosal break

uT3 lesions

uT3 lesions (Figs. 6, 7) are locally advanced cancers that penetrate the full thickness of the muscularis propria and into the perirectal fat. Sonographically, uT3 lesions are depicted by disruption of the submucosa, with thickening of the muscularis propria and breech of the hyperechoic white line, indicating penetration into the perirectal fat. There is a high incidence of lymph node metastasis in uT3 lesions: up to 66% [14]. Deep uT3N0 and uT3N1 lesions should be treated with neoadjuvant therapy prior to radical resection. The accuracy of ERUS in evaluating T3 lesions ranges from 70% to 81% [24].

uT4 lesions

uT4 lesions (Fig. 8) invade local adjacent structures such as the prostate, vagina, uterus, cervix, bladder, pelvic sidewall, or sacrum. Pelvic MRI may complement ERUS in staging T4 lesions, as the accuracy of ERUS

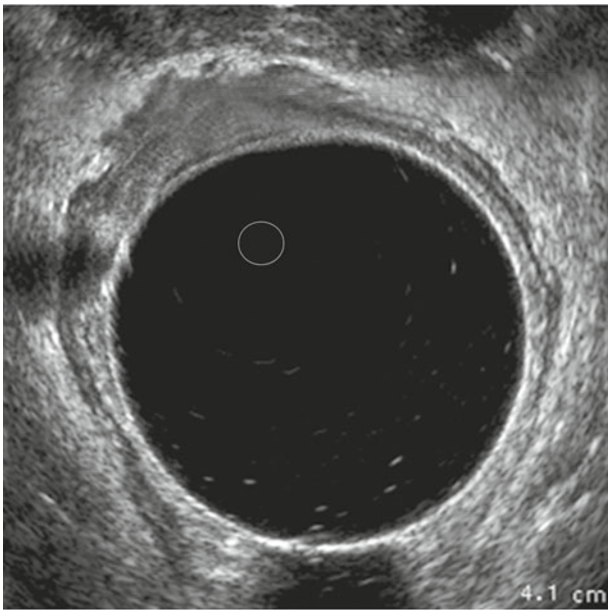

Fig. 6. uT3 lesion. An early uT3 lesion in the right anterior aspect of the rectum. There is a break in the submucosa, thickening of the muscularis propria and disruption of the hyperechoic white line, indicating penetration into the perirectal fat

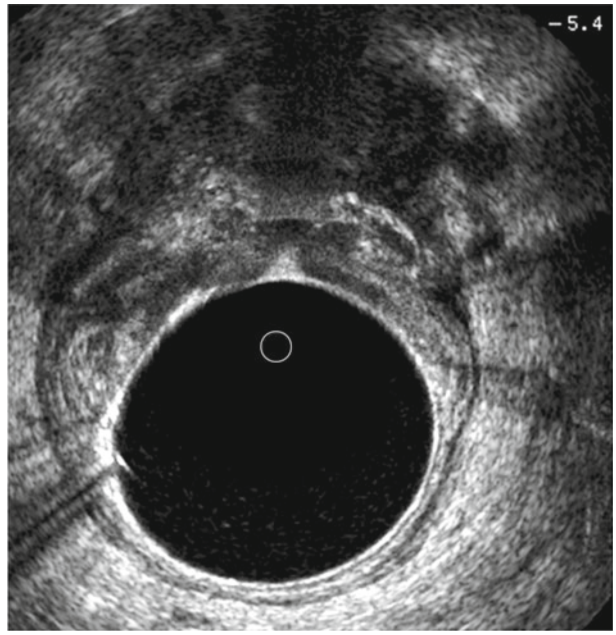

Fig. 8. uT4 lesion. A uT4 lesion in the anterior rectum. The lesion invades anteriorly into the prostate

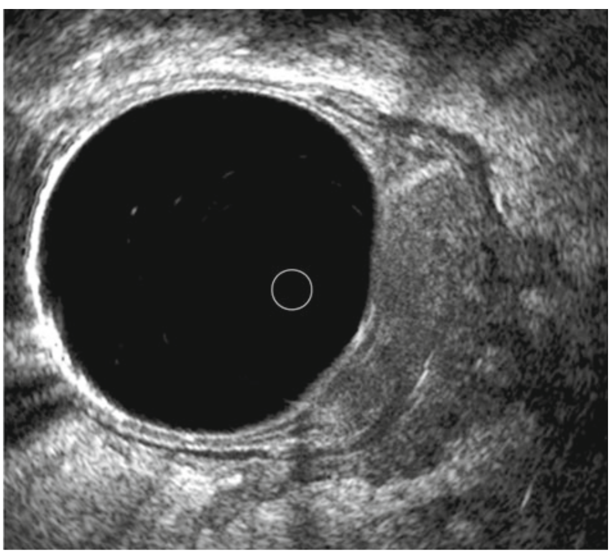

Fig. 7. Deep uT3 lesion. A deep uT3 lesion in the left lateral aspect of the rectum. There is 'thumbprinting" and clear invasion into the perirectal fat

is only 50% [8]. Sonographically, there is a breach of the normal hyperechoic interface between tumor and adjacent organ. Treatment of T4 lesions requires neoadjuvant chemoradiation therapy and en bloc resection for cure. Neoadjuvant therapy may decrease tumor size and increase resectability. In specialized centers, intraoperative radiation therapy along with preoperative radiation may improve local control of T4 cancers [25].

Nodal involvement

The presence of metastatic versus inflammatory lymph nodes is associated with survival rates and local recurrence. Lymph nodes can be detected by ERUS. This also helps with decision-making regarding preoperative planning for rectal cancer. Inflammatory lymph nodes appear hyperechoic and are generally larger, with an irregular contour. ERUS accuracy for evaluating lymph node metastasis ranges from 50% to 88% [15, 26–28]. Tio and Tygat described the hypoechogenic pattern of malignant lymph nodes in 1986 [29]. Generally, malignant lymph nodes are hypoechoic and located in the proximal mesorectum or adjacent to the primary tumor (Fig. 9). Hypoechoic lymph nodes larger than 5 mm are highly suspicious for metastases. However, there is no specific size cutoff for metastatic disease. Herrara and Ornelas found that two-thirds of metastatic lymph nodes in pathologic specimens were smaller than 5 mm [30]. Katsura demonstrated that lymph nodes measuring 4 mm or less were metastatic in 18% of specimens [31]. In another study by Sunochi et al. lesions as small as 1–3 mm at the margin of the rectum were described as "small spot signs", associated with massive venous or histologic lymphatic invasion [32].

Lymph node staging with ERUS has potential errors. False positive results (overstaging) may occur due to inflammatory lymph nodes. On cross-sectional examination blood vessels and perirectal fat may be confused

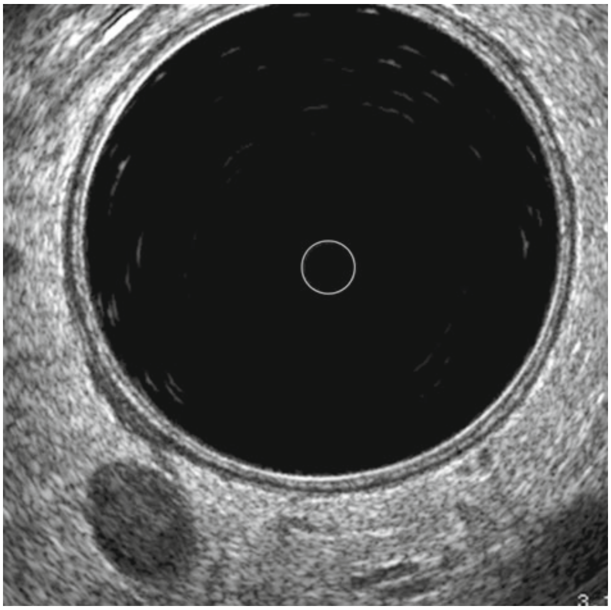

Fig. 9. N1 nodal involvement. A metastatic lymph node can be seen in the right posterior aspect of the mesorectum. Typically, the metastatic node is round and hypoechoic

with positive lymph nodes. There may also be islands of tumor outside the bowel wall that are difficult to differentiate from involved nodes.

Lymph node understaging (false negatives) may also pose a problem. Lymph node micrometastasis cannot be detected by ERUS. Lymph nodes can remain unidentified when they are outside the focus of the imaging transducer, especially nodes located in the proximal mesorectum.

Accuracy of ultrasound in diagnosis of rectal cancer

Overstaging depth of wall invasion has reportedly been between 11% and 18% [15, 33]. Understaging depth of invasion occurs less frequently, ranging from 5% to 13%. Overstaging depth of invasion may occur if the tumor is surrounded by inflammation, if there is hemorrhage in the rectal wall following biopsy, or if the patient has undergone preoperative radiation. Understaging of disease occurs in near-obstructing stenotic tumors beyond which the endosonic probe cannot be passed.

Lymph node overstaging occurs in 5% to 33% of cases [34]. Overstaging occurs with tumor deposits in the mesorectum, blood vessels, and inflammatory lymph nodes. Lymph node understaging occurs in 2% to 25% of cases and is usually due to the inability to detect lymph node micrometastasis [15, 35].

ERUS is highly operator-dependent. Accuracy improves with experience [49]. Misinterpretation of ultrasound images may be due to artifact secondary to balloon wall separation, poor bowel prep, or retained air producing shadowing artifact; malpositioning from the suggested 90 degree angle with respect to the region of interest; or manipulation of the bowel wall via biopsy, cauterization, or excision affecting the image and accuracy of sonographic staging [50]. The accuracy of ERUS after neoadjuvant therapy is decreased. Radiation-induced changes, including inflammation and fibrosis, obscure the planes of the rectal wall. There are high rates of overstaging with ERUS after neoadjuvant therapy [51]. In one study from Rau et al. misinterpretation of the T stage correlated with downstaging [52]. Gavioli et al. described inconsistency in tumor wall staging due to fibrosis following neoadjuvant therapy. The extent of fibrosis in the rectal wall is an indication of the depth of residual cancer and tumor deposits present in the fibrosis. However, a definite echo pattern could not be correlated on ERUS [53]. Vanagunas et al. reported 38% overstaging and 14% understaging in any ERUS T-stage determination following neoadjuvant therapy [54]. This same limitation applies to other imaging tools such as CT and MRI [55]. Currently, none of the conventional imaging modalities (ERUS, CT, MRI) reliably detect complete response and, therefore, they fail to identify the subgroup of patients who can safely avoid radical surgery [56].

Table 1: Accuracy of ERUS in the staging of rectal cancer

Author	Year	*n*	Accuracy (%) T stage	Accuracy (%) N stage
Hildebrandt and Feifel [6]	1985	25	92	NA
Romano et al. [36]	1985	23	87	NA
Hildebrandt et al. [37]	1986	76	88	74
Holdsworth et al. [33]	1988	36	86	61
Beynon et al. [38]	1989	100	93	83
Dershaw et al. [39]	1990	32	75	72
Glaser et al. [40]	1990	86	88	79
Glaser et al. [41]	1990	110	94	80
Jochem et al. [42]	1990	50	80	73
Milsom et al. [43]	1990	52	83	83
Orrom et al. [28]	1990	77	75	82
Katsura et al. [31]	1992	112	92	NA
Herzog et al. [24]	1993	118	89	80
Sentovich et al. [44]	1993	24	79	73
Deen et al. [45]	1995	209	82	77
Adams et al. [46]	1999	70	74	83
Garcia-Aguilar et al. [8]	2002	545	69	64
Marusch et al. [47]	2002	422	63	NA
Manger and Stroh [48]	2004	357	77	75

ERUS in postoperative follow-up

Local recurrence is a difficult problem following treatment of rectal cancer. ERUS has been shown to successfully identify asymptomatic recurrent disease [34, 57–59]. Local recurrence rates are reportedly between 4% and 30% after curative rectal cancer surgery [60, 61]. In combination with digital rectal examination and endoscopic surveillance, ERUS may significantly improve the detection of recurrent lesions and improve the ability to diagnose recurrent neoplasms by 30% [62]. Recurrent tumor appears as a circumscribed hypoechoic lesion surrounding the anastomosis. The rectal wall may appear intact with surrounding fibrosis. A caveat is that the postoperative changes adjacent to the anastomosis make interpretation of ERUS difficult following radical excision. Therefore, we do not routinely use ERUS in the postoperative period for patients who have undergone radical surgery.

The role of ERUS after local excision of rectal cancer, however, is warranted. Baseline ultrasound after 3 months is the preferred tool for detecting postoperative scarring and evaluating changes in subsequent followup examinations. On surveillance, enlarged lesions are more likely to represent recurrent tumor, and biopsy can then be taken to confirm or rule out recurrent disease. ERUS followup is particularly useful for patients treated with local therapy for rectal cancer as early diagnosis of tumor recurrence is imperative for curative salvage surgery. To date, the optimum interval and length of serial examinations has yet to be determined. At MSKCC, in complement with clinical examination, proctosigmoidoscopy, and CEA levels for patients who have undergone local excision for rectal cancer, we practice ERUS every 4 months for 1–2 years after surgery, and every 6 months for the next 3 years.

Endoanal ultrasound

Evaluation of the anal canal is done with digital rectal examination, anoscopy, and endoanal ultrasound. The endoanal ultrasound equipment is similar to that used for ERUS. We use the same B & K scanner with 1850 rotating probe and 10 MHz transducer. In lieu of the latex balloon, a translucent plastic cap (B-K type WA0453) is placed over the transducer and filled with water to provide an acoustic medium. The transducer maintains contact with the anal canal and a small pinhole in the apex allows escape of air. The patient is placed in the left lateral decubitus position, and lubrication with water soluble gel is used to introduce the cap into the anal canal. When the cap is no longer visible, the transducer will be at the level of the upper anal canal. The upper anal canal is characterized by the puborectalis, which appears as a hyperechoic U-shaped structure oriented posteriorly and laterally (Fig. 10). The mid anal canal is characterized by the hypoechoic internal anal sphincter, surrounded by the hyperechoic external anal sphincter (Fig. 11). The perineal body can be measured at the level of the mid anal canal; normal measurement ranges from 10–15 mm, the lower limit of normal being 8 mm. In female patients this measurement is done with a gloved finger placed within the vagina against the rectovaginal septum and ultrasound probe. The distal anal canal is characterized by the absence of the internal sphincter. At the level of the distal anal canal, only the

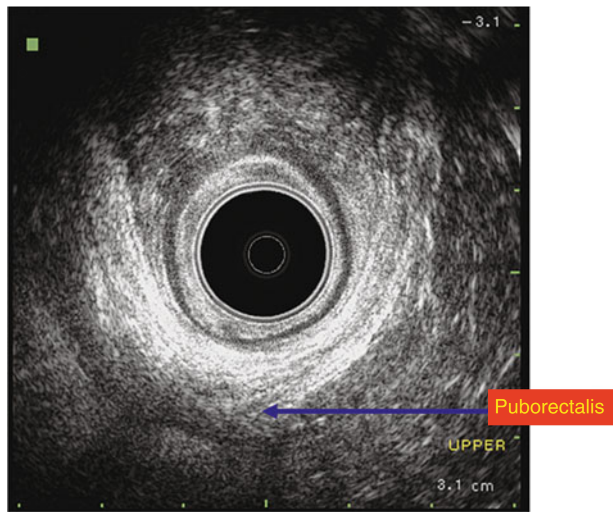

Fig. 10. Upper anal canal. Endorectal ultrasound image of a normal anal canal. Note the "sling-like" appearance of the puborectalis

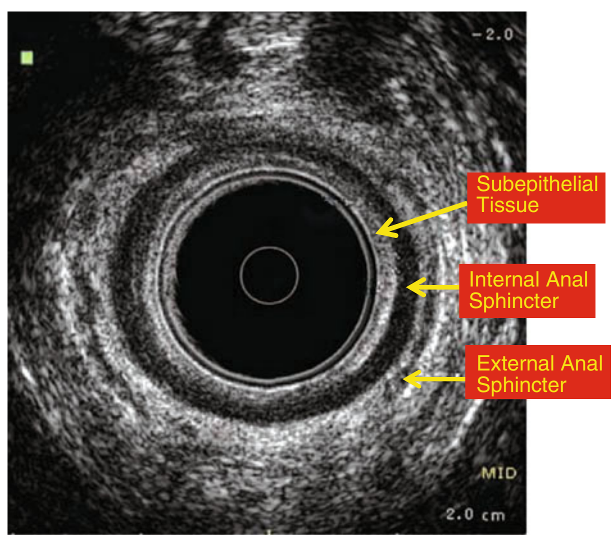

Fig. 11. Mid anal canal. Normal mid-anal canal as it appears on endorectal ultrasound. Hallmarks of the mid-anal canal are the internal and external anal sphincters

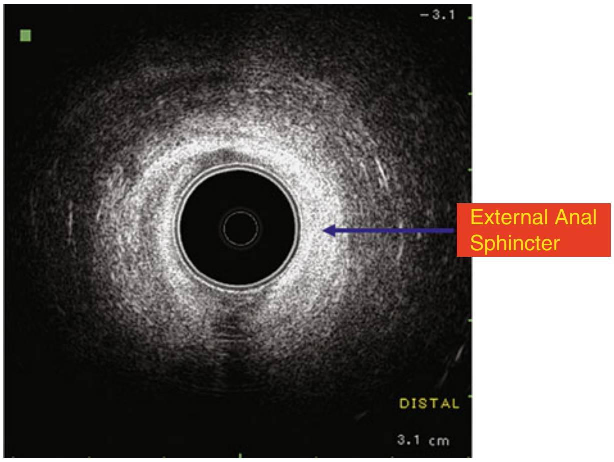

Fig. 12. Distal anal canal. Normal distal anal canal, as it appears on endorectal ultrasound. Note that only the external anal sphincter and surrounding soft tissues can be seen

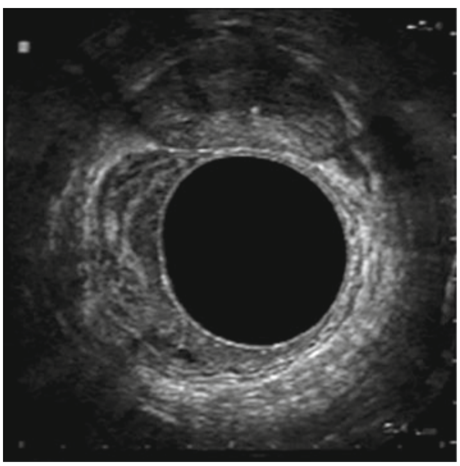

Fig. 13. Tumor amenable to intersphincteric resection. Note intersphincteric tumor in the upper anal canal

external anal sphincter and surrounding soft tissues are seen (Fig. 12). It is important to accurately assess distal rectal cancer, as there may be opportunity to offer a sphincter-saving procedure. ERUS/ERAS have great value in predicting the lateral clearance and outcome for patients with adenocarcinomas located in the lower third of the rectum [63]. The technique for intersphincteric resection of low rectal cancers (Fig. 13) with good oncologic and functional outcomes has previously been described [64, 65]. Sphincter-preserving procedures are now possible in the setting of distal rectal cancer, with preoperative chemoradiation for stage II and III rectal cancers followed by intersphincteric resection of the distal tumor, without compromise of circumferential or distal margins, or oncologic outcome [66, 67]. Intersphincteric dissection of rectal tumors as low as 3 cm from the anal verge can be achieved with complete microscopic resection (R0) and negative distal and circumferential margins [68]. Tumor involvement of the external sphincter complex itself, however, is an absolute contraindication to sphincter-saving surgery [69–72].

EAUS for anal canal neoplasms [5]

In addition to evaluating low-lying rectal cancers, EAUS is useful for evaluating malignant neoplasms of the anal canal (including adenocarcinomas). Squamous cell carcinoma is the most common anal canal malignancy. EAUS is invaluable in accurate assessment and followup of patients with SCC of the anal canal [73]. EAUS may be used to evaluate the extent of tumor involvement of the sphincter muscles, and to examine the mesorectum for metastatic lymph nodes.

Anal canal tumors are staged according to the AJCC classification, below.

Primary tumor (T)

TX: The primary tumor cannot be evaluated.
T0: There is no tumor.
Tis: Refers to carcinoma *in situ* (which is very early cancer that has not spread).
T1: The tumor is no larger than 2 centimeters (cm).
T2: The tumor is larger than 2 cm but not larger than 5 cm.
T3: The tumor is larger than 5 cm.
T4: The tumor has invaded other organs, such as the vagina, urethra, or bladder.

Regional nodes (N)

NX: Regional lymph nodes cannot be evaluated.
N0 (N plus zero): There is no regional lymph node metastasis.
N1: Cancer has spread to the perirectal (around the rectum) lymph nodes.
N2: Cancer has spread to the internal iliac (pelvic) and/or the inguinal lymph nodes (lymph nodes in the groin just under the skin surface) on the same side of the body.
N3: Cancer has spread to the perirectal and inguinal lymph nodes and/or the internal iliac and/or inguinal lymph nodes on both sides of the body.

Distant metastasis

MX: Distant metastasis cannot be evaluated.
M0 (M plus zero): There is no distant metastasis.
M1: There is metastasis to other parts of the body.

Stage grouping

Stage 0: Abnormal cells are identified in the first layer of the lining of the anus only. The abnormal cells may become cancer. This stage is also called carcinoma *in situ* (Tis, N0, M0).

Stage I: The tumor is no larger than 2 cm, with no spread to lymph nodes or other parts of the body (T1, N0, M0).

Stage II: The tumor is larger than 2 cm, with no spread to lymph nodes or other parts of the body (T2 or T3, N0, M0).

Stage IIIA: The tumor may be any size and has spread to nearby lymph nodes or to organs, such as the vagina, urethra, and bladder (T1, T2, T3; N1, M0; or T4, N0, M0).

Stage IIIB: The tumor may be any size and has spread to nearby lymph nodes or organs, lymph nodes in the pelvis and/or groin, or to lymph nodes near the rectum, in the groin and/or on both sides of the pelvis or groin (T4, N1, M0; or Any T, N2 or N3, M0).

Stage IV: The tumor may be any size and has spread to lymph nodes and to distant parts of the body (Any T, Any N, M1).

Anal canal tumors may also be staged according to the depth of invasion, as proposed by Tarantino and Berstein. uT1 is confined to the submucosa. uT2a invades only the internal sphincter. uT2b penetrates into the external anal sphincter. uT3 lesions invade through the sphincter complex into the perianal tissue, and uT4 into the adjacent structures [74]. Giovanni et al. proposed a slightly different ultrasound staging system in which uT2 lesions involve the internal sphincter and uT3 lesions invade the external sphincter [75].

The value of EAUS in detecting residual tumor and local recurrence after treatment is supported by small prospective and retrospective studies [76, 77]. In surveillance of anal cancer, EAUS may identify a percentage of patients who fail chemoradiotherapy but can undergo salvage APR, with a reasonable chance for cure [78].

Conclusions

With the introduction of ERUS/EAUS, the clinician gained another tool to assess low rectal and anal canal cancer. The staging accuracy of DRE for rectal cancer ranges from 57% to 83% [4]. The accuracy of T and N staging by CT scan is 73% and 66%, respectively. For MRI, the accuracy of T and N staging is 82% and 74%, respectively. For MRI with endocoil, the accuracy of T and N staging is 84% and 82%, respectively. Overstaging of tumor depth by CT, MRI, and MRI with endocoil is 7%, 13%, and 6% respectively. In experienced hands, ERUS allows for a T staging accuracy of 87%, an N staging accuracy of 74%, overstaging of tumor depth in 11%, and understaging of tumor depth in 5% [15]. ERUS has proven to be invaluable in preoperative local staging of rectal and anal canal cancers. It is useful in preoperative planning of intersphincteric resection for low-lying rectal cancers. ERUS is of great use in surveillance after treatment of rectal and anal disorders, and it is extremely useful in the evaluation of fecal incontinence and a host of other benign anorectal conditions. ERUS has made a valuable contribution to the evaluation and management of many anorectal diseases. It is an important tool that should be used by all practicing colon and rectal surgeons.

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Intersphincteric resection: MRI for staging

Michael Urban

Introduction

With the advance of surgical therapy of rectal carcinoma and improvement of adjuvant therapies the challenges for preoperative staging methods have grown over the last years. The radiologists understanding of rectal carcinoma is constantly evolving. The need of precise staging before operative therapy has lead to refinements in the technique of staging examinations. The election of patients in need of neoadjuvant therapy, reevaluation after therapy, radiation therapy planning and assessment of postoperative changes and recurrence are challenges in the diagnostic workup of patients with rectal cancer. Magnetic resonance imaging (MRI) is now routinely used for preoperative staging of rectal cancer. It provides accurate assessment of the tumor and the surrounding mesorectal fascia as well as precise depiction of important anatomic structures as for example the structures of the pelvic floor and the anal sphincter in tumors of the low rectum. On the other hand evaluation of nodal metastases is still a diagnostic challenge with MRI.

To take full advantage of the possibilities of the method, knowledge of operative techniques, indications for adjuvant therapy and about the typical MRI appearance of the tumor itself and its spread to adjacent structures are paramount. A standardized examination technique and description is of utmost importance to provide the surgeon with all necessary information.

Examination technique

Early MRI studies used body coils which lacked the resolution to differentiate the layers of the rectal wall and therefore had no advantage over CT. The introduction of endorectal coils improved image resolution and lead to more consistent T Staging with accuracies between 71% and 91% [1]. Endoluminal MRI proved to be as accurate as Endorectal Ultrasound (ERUS) for the staging of superficial tumors [2–4]. However, limitations in the field of view, lack of depiction of the mesorectal fascia higher up due to signal drop and problems with positioning of the coil especially in tumors of the low rectum reaching to the anal canal, with reported failed insertion rates of up to 40% [5] have made the use of these coils questionable.

The development of phased array coils and subsequent introduction of high resolution MRI showed excellent results in discrimination of the mesorectal fascia and the depth of tumor invasion. With this the prediction of a tumor free circumferential resection margin (CRM) is possible [6, 7]. These findings lead to the development of a standardized imaging protocol that proved to be accurate in the multicentre European MERCURY study [8].

Bowel preparation, filling of the rectum or the use of intravenous contrast enhancement is now no longer recommended for staging of rectal cancer [7]. A 1.5-T system with phased array coils is used A Sagittal T2 weighted turbo spin echo sequence from one pelvic sidewall to the other is first performed to show the extent of the tumor and to be able to plan high resolution axial imaging (Fig. 1a).

Axial large-field-of-view sections of the whole pelvis follow.

The 3rd series consists of axial high-resolution T2 weighted thin section images (3 mm) through the cancer and adjacent structures perpendicular to the long axis of the tumor (Fig. 1b). In tumors of the low rectum a high spatial resolution T2-weighted series showing the pelvic floor, sphincter complex, intersphincteric plane and the tumor relation to these structures and the pelvic wall is performed (Fig. 1c).

As lymphatic drainage is upwards in the mesorectum at least 5 cm coverage above te upper edge of the tumor with high resolution is recommended [9].

Earlier studies proposed different approaches. Rectum distension with water or negative MRI contrast media, air insufflation or ultrasound gel and subsequent T1 weighted imaging, before and after i.v. administration of Gadolinium have been performed successfully [10–12]. Especially for staging of sphincter infiltration these

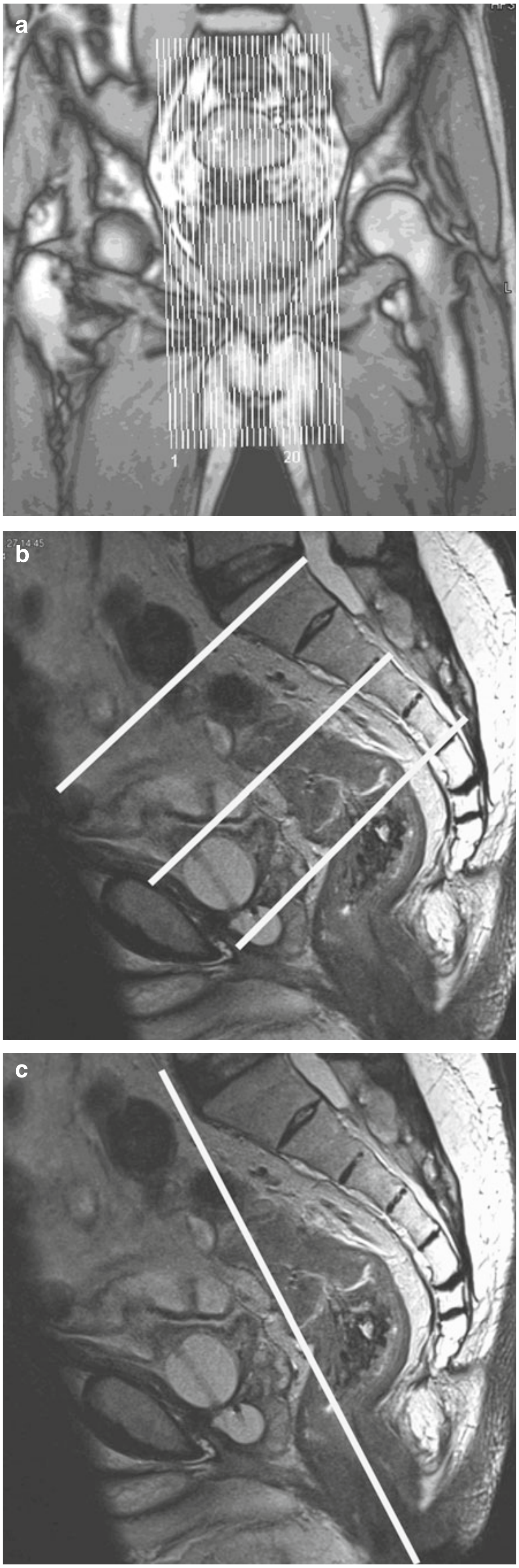

Fig. 1. (a) Positioning of the sagittal T2 weighted sequence from one pelvic sidewall to the other. (b) Paraxial T2-weighted Slices angled 90° to the long axis of the tumor. (c) Orientation of the coronal images in tumors of the low rectum

techniques have proved to be accurate [11, 12]. T1 weighted imaging after contrast can still be helpful in certain cases. However, studies have shown that staging of rectal cancer is not improved by Gadolinium enhanced T1-weighted imaging [13, 14].

Recent studies of prediction of CRM involvement during restaging of irradiated rectal cancers by using T2-weighted and Gd enhanced T1-weighted imaging demonstrated high diagnostic accuracy in comparison with that of studies using only T2-weighted imaging [15]. However, this was explained as being caused by differences in study population and the cutoff level more than by the additional gadolinium enhanced study [16].

Anatomical considerations

Exact preoperative knowledge of the extent of spread in relation to important anatomical structures is important in planning surgery as the surgical approach may be altered or preoperative therapy as chemoradiation may be used. Brown et al. proved in 2004 that thin section MRI performed with a pelvic phased-array coil can depict these structures essential for preoperative staging with high accuracy [7]. Fine details of the rectal wall, mesorectum, anal sphincter and the pelvic sidewall as well as fourth order branches of the IMA and lymph nodes down to a size of 2 mm can be identified constantly.

The important structures for staging are

1. the peritoneal reflection
2. the urogenital septum
3. the nerve plexuses within the pelvis
4. the mesocolon, mesorectum, mesorectal fascia, and retroperitoneal fascia
5. the rectal wall
6. the pelvic floor and sphincter apparatus

The peritoneal reflection

The greatest part of the rectum is located extraperitoneally, only the anterior upper rectum is covered by a thin layer of visceral peritoneum around the front and sides down to the peritoneal reflection [17]. The peritoneal reflection is normally found about 7 to 9 cm from the anal verge (Fig. 2). In women it may ly lower (at 5, 7 to 5 cm) [18]. It can be seen on sagittal MRI as a low-signal –

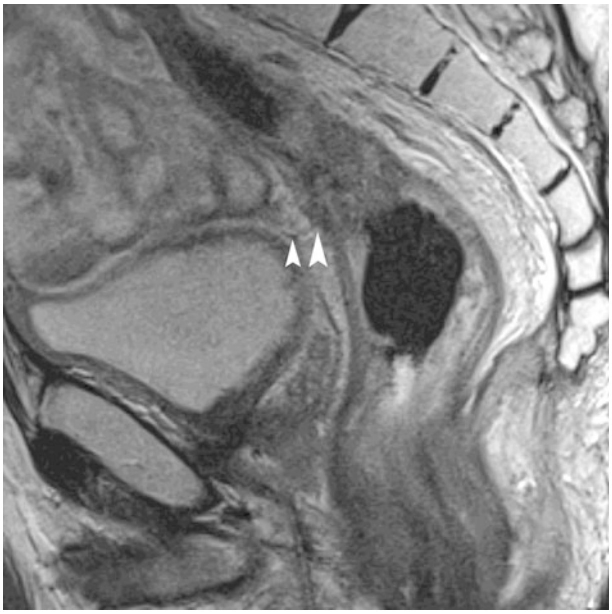

Fig. 2. Sagittal T2 weighted image showing the peritoneal reflection appearing as a thin line from the bladder to the midrectum

intensity line anterior to the rectum, on transverse images it shows a V-shaped appearance on the anterior aspect of the rectum.

The urogenital septum

Denonvilliers' fascia or the urogenital septum is an avascular sheath that originates from the embryonic pelvic floor (Fig. 3). It divides the posterior hindgut (rectum and perirectal structures) from the urogenital organs. It consists of collagenous and elastic fibers and smooth muscle cells mixed with nerve fibers. In the embryonic period, the septum is formed by a local condensation of mesenchymal connective tissue. In the male, it is seen as a shiny anterior surface of the rectum (Denonvilliers fascia). In women, it is called the rectovaginal septum. On sagittal MRI, it can be traced up to the peritoneum superiorly as a low signal layer [4, 19].

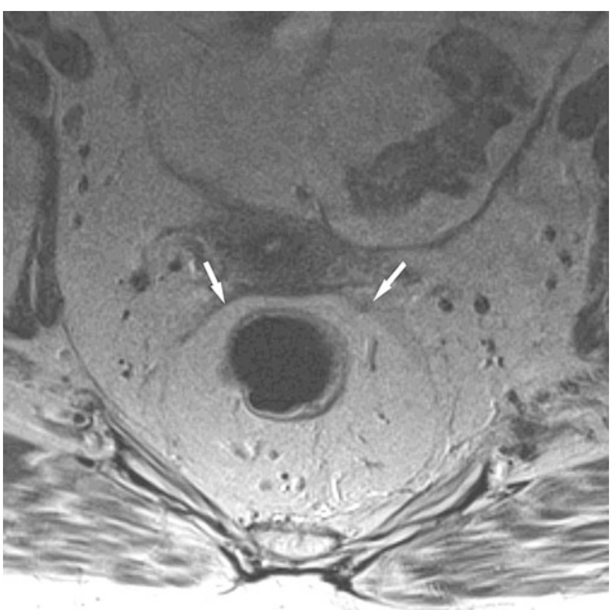

Fig. 3. The urogenital septum (or Denonvilliers Fascia) is shown as hypointense bandlike structure on this axial T2-weighted image (arrows)

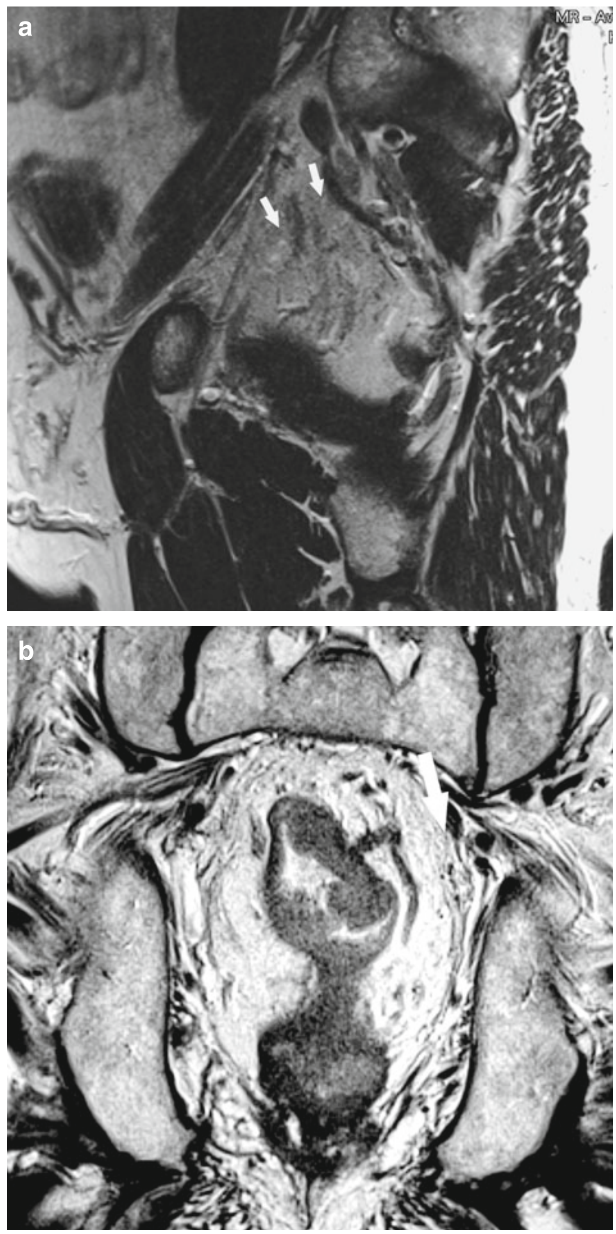

Fig. 4. The pelvic nerve plexuses are shown on these sagittal (**a**) and coronal (**b**) images as parasagittal tubular structures in the lateral pelvis (arrows)

The pelvic nerve plexuses

The autonomic nerve supply to the pelvic viscera comes from two main sources. The sympathetic supply descends around the aorta and forms the hypogastric plexus below the aortic bifurcation. The superior hypogastric plexus divides into two plexiform hypogastric nerves which descend 1–2 cm below each ureter to join the inferior hypogastric plexus. The hypogastric nerves are directly related to the retrorectal space, lying on the presacral fascia and often adherent to the visceral fascia when the rectum is pulled anteriorly [20]. During pelvic dissection it is essential to preserve these nerves. The parasympathetic supply arises as the nervi erigentes from S2, S3, and S4. They run laterally behind the parietal fascia before crossing it to join the inferior hypogastric plexus. The inferior hypogastric plexus lies sagittally. In the male, its mid-point is marked by the tip of the seminal vesicle, and in the female its anterior half lies against the upper third of the vagina [21]. It lies in a plane medial to the vessels on the pelvic side wall. The plexus forms a meshwork up to 4 cm long in the sagittal plane and can be visualised on MRI on parasagittal or paracoronal views (Fig. 4).

The mesorectum and mesorectal fascia

The mesorectum is a distinct compartment that derives from the embryologicalhindgut and surrounds the rectum as a fat containing layer of connective tissue and vessels and draining lymphatics [17, 18, 20]. It is covered by a fascial covering derived from the visceral peritoneum– the mesorectal fascia (Fig. 5). This layer is enclosing the mesorectum, and thus anterior to the retrorectal space, variously named the visceral fascia of the mesorectum, fascia propria of the rectum, or presacral wing of the hypogastric sheath. The mesorectal fascia is appreciated best on axial section and is seen as a low signal linear structure surrounding the mesorectum and is consistently depicted on thin slice MR imaging [4]. The mesorectum is demonstrated as a high signal intensity (fat signal) envelope surrounding the rectum, containing vessels which are depicted as low signal (signal void produced by blood flow). Lymph nodes are shown as high signal (due to high fluid content) ovoid structures. Small nerves within the mesorectum are not visualized but interlacing connective tissue within the mesorectum is shown as low signal intensity strands [4] (Fig. 5a, b).

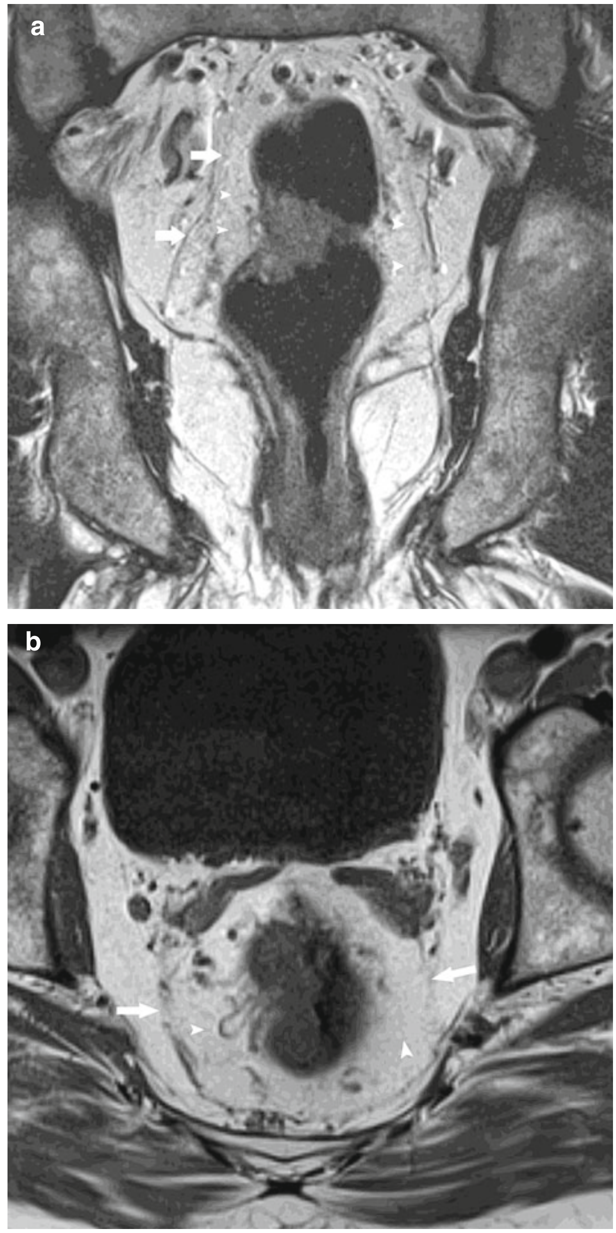

Fig. 5. Axial (**a**) and coronal (**b**) T2 weighted images showing the mesorectum and mesorectal fascia. The mesorectum is depicted as a high signal intensity fat containing space with strands of connective tissue (arrowheads), the surrounding mesorectal fascia is shown as linear hypointense structure (arrows)

The normal rectal wall

In cross section, the rectal wall consists of the mucosal layer, the muscularis mucosae, submucosa, and the muscularis propria which is built of the circular and outer longitudinal layers. The two layers are separated by a thin layer of connective tissue containing the neuromyenteric plexus. MRI shows the mucosal layer as a fine low signal intensity line with the thicker, higher signal submucosal layer underneath. Sometimes the muscularis propria can be depicted as two distinct layers. The outer muscle layer has an irregular corrugated appearance and there are frequently interruptions within it caused by vessels entering the rectal wall. The perirectal fat appears as high

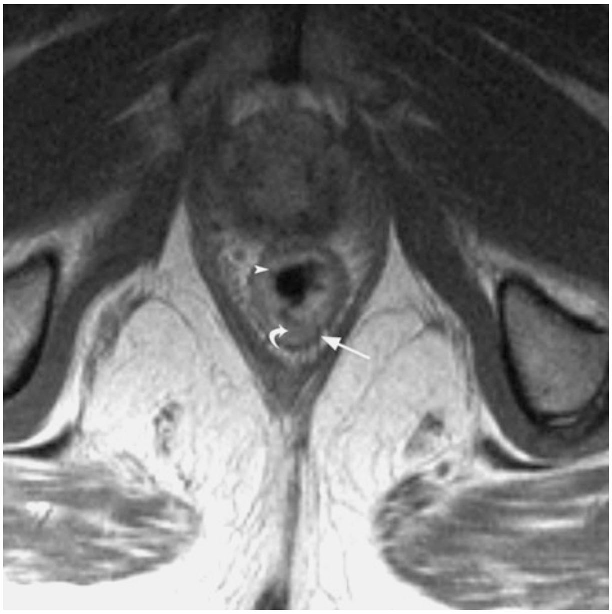

Fig. 6. The normal rectal wall as seen on axial T2-weighted images

signal surrounding the low signal of the muscularis propria (Fig. 6).

The pelvic floor and anal sphincter

The levator ani forms a symmetrical array of paired striatal muscles – puborectalis, pubococcygeus, ileococcygeus and –variably-ischiococcygeus muscle. The puborectalis forms a U-shaped, strong sling of muscle, that pulls the anorectal junction anteriorly to the pubis. An angulation between the rectum and anal canal results (anorectal angle). It relaxes during defecation, thereby widening the anorectal angle and straightening the rectum [18, 22] (Fig. 7).

The anal canal has been studied with endorectal and pelvic array MRI in various anatomic studies [23–25]. It consists of two partially overlapping tubes, the internal and external anal sphincters. The internal sphincter is cigar shaped and shorter than the external sphincter. It extends above the external sphincter and the puborectalis wraps around it upper portion. It has intermediate signal on T2 weighted images and enhances on post Gadolinium T1-weighted sequences.

Between the internal and external sphincters lies the intersphincteric space, which is a fat containing thin layer, depicted with high signal on all sequences. Fibres from the superficial fascia of the levator ani join with the longitudinal muscle of the rectum. This structure continues downwards, dividing the intersphincteric space into an inner and outer space. The lower end of this conjoint longitudinal coat inserts into the rolled cuff of the subcutaneous portion of the external sphincter.

Outside the intersphincteric plane lies the external anal sphincter, also formed by circular muscle fibres, extending from the puborectalis muscle to the anal verge. It is separated form the puborectalis by a notch of fat, best seen on T2 weighted coronal images. The signal of the external sphincter is different to the internal sphincter, it is lower on T2 weighted images and shows a lower degree of enhancement after Gadolinium injection.

The external sphincter shows a segmented structure on imaging. The middle part has extensions anteriorly and posteriorly, depicted as intermediate signal fibrous structures. The subcutaneous part of the external sphincter can be seen encircling the anal verge on sagittal imaging. 'In the axial view it is incomplete posteriorly. It has fibers to the coccyx posteriorly and hooks under the bulbospongiosus anteriorly in men. On coronal images the lowest part turns upwards forming a cuff which limits the intrasphincteric space. The conjoint longitudinal coat anchors here.

The puborectalis mucle is a loop of muscle at the upper border of the external sphincter, attached to the posterior aspect of the pubic bone. It maintains the angle between the rectum and anal canal by forming a sling at the anorectal junction. On axial views it is open anteriorly. On sagittal paramedical views it can be seen as oblique muscular structure angling down from the pubic bone. On coronal views it is seen at the lower end the levator muscles (Fig. 7).

Inside the internal sphincter lies the mucosal surface, which forms a star like pattern on axial images. It appears bright on T2-weighted images.

Tumor morphology and T staging

Criteria for identifying the layers of the bowel wall and T staging tumor were originally proposed from work using endoluminal coils [26–29]. However, these studied small groups of patients, and both the image interpretation criteria and image acquisition parameters were not consistent. In particular, the observation by Schnall et al. [30] that "non-luminal irregularity" was an unreliable sign of T3 tumor contradicted observations made by Murano et al. [26], Joosten et al. [27], Pegios et al. [28], and Vogl et al. [29] that irregularity and spiculation of the outer margins of the muscularis propria indicated tumor infiltration into perirectal fat. In addition, Pegios et al. [25] and Vogl et al. [26] suggested that intravenous contrast enhancement was useful in identifying tumors with spread beyond the bowel wall. Conversely, Okizuka [31] showed that intravenous contrast enhancement resulted in overstaging owing to perirectal vessel enhancement. There is now Agreement between most authors, that T2 weighted

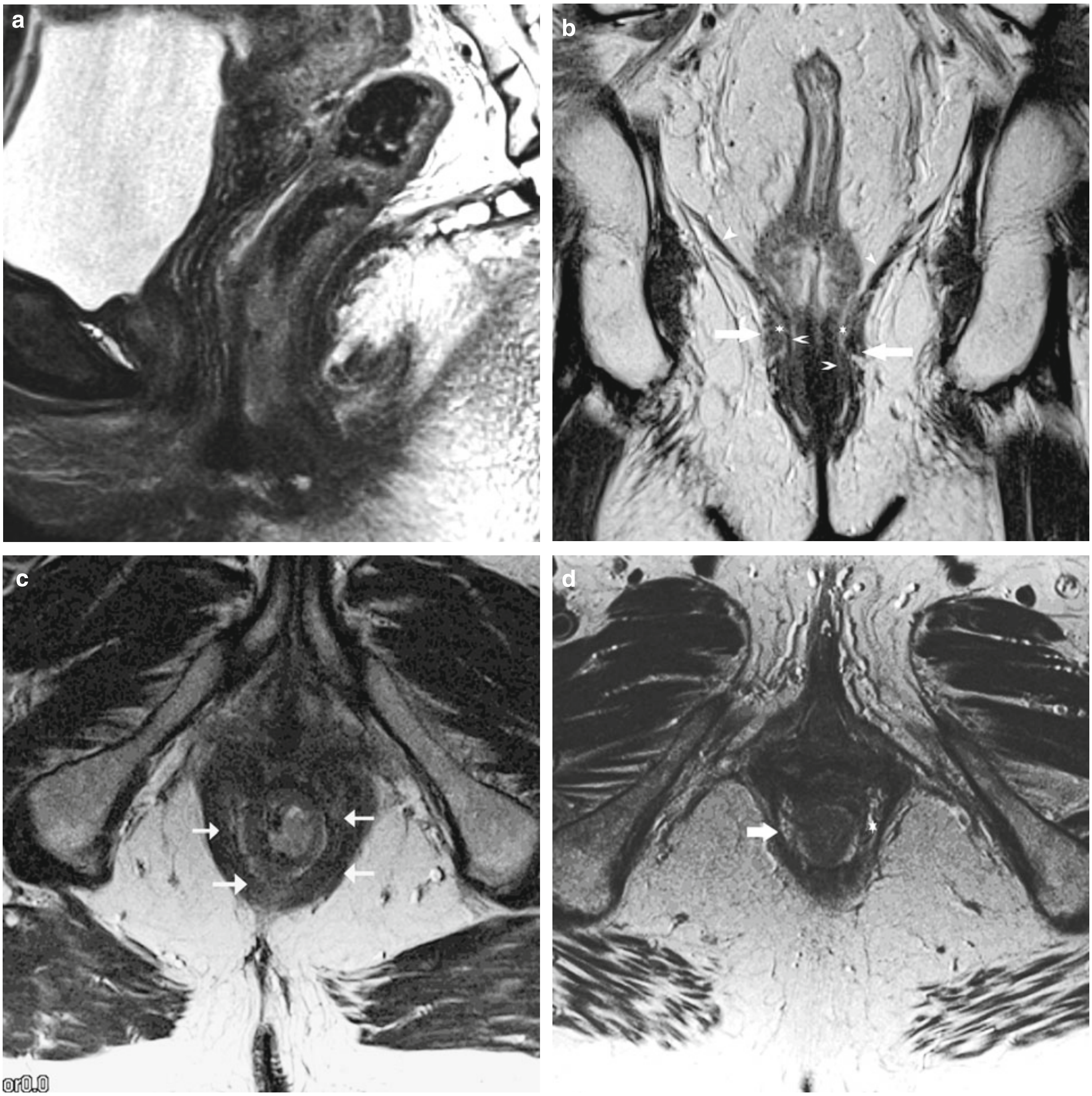

Fig. 7. Sagittal (**a**), coronal (**b**) and axial (**c**, **d**) images of the sphincter and anal canal. The levator ani is shown as funnel like muscular structure (arrowheads). The puborectalis sling surrounds the anorectal junction as thick hypointense muscular band (small arrows). The external sphincter is depicted with its different parts with hypointense signal (large arrows), medial to it the intersphincteric plane can be seen as hyperintense zone (asterisxs). The internal sphincter is shown as continuation of the rectal wall musculature (open arrows)

images provide the best contrast between tumor and rectal wall.

Stage T1 on MRI is defined as preservation of the submucosal layer. This, if it can be identified is a helpful feature with high positive predictive value. It has to be noted, that loss of the high signal mucosal layer will not allow distinction between a T1 and a T2 lesion since microscopic infiltration into circular muscle (pT2) and complete replacement of the submucosal layer by tumor (pT1) have the same appearance on MRI [4]. The same is true for the differentiation of tumors occupying the full thickness of the bowel wall (pT2) and such with sub-millimetre extension through the outer longitudinal muscle layer.

Most commonly rectal tumors present as ulcerating lesions with a central depression and raised rolled edges. This feature can be recognized on high resolution MRI (Fig. 8). In less advanced cases, an elevated plaque of intermediate signal intensity projects into the lumen forming a U-shaped thickened disc that corresponds to a semi-annular plaque of tumor on histology sections. As tumors become more aggressive, they invade the deeper layers of

Fig. 8. Axial T2-weighted image. Ulcerating tumor in an axial view showing bowl like appearance with central depression and raised, rolled edges

Fig. 9. T3 tumor invading the mesorectal fat with a broad and rather distinct margin (arrow)

the bowel wall and beyond, and develop the capacity for lymphatic and vascular invasion. Rectal tumors commonly invade through the bowel wall into the perirectal fat with a well-circumscribed margin. Sometimes, the pattern of spread is infiltrative with ill-defined borders. Malignant epithelium can be found between normal structures so that no distinct border of the tumor can be identified. This pattern of spread has long been known to worsen prognosis [32–34]. Regardless of differentiation, colorectal tumors unlike upper gastrointestinal tumors rarely show submucosal or intramural spread beyond their macroscopic borders. This characteristic is important in the surgical planning of distal resection margins [8–10]. These two histopathology patterns are demonstrable on MR images and therefore are used as criteria for identifying T3 spread into perirectal or pericolonic fat. Tumor extension beyond the bowel wall is manifested as intermediate signal intensity spreading either with a broad-based pushing margin (Fig. 9) or with finger-like projections forming nodular extensions into perirectal or pericolonic fat. Spiculation, which is different in appearance has been described as a manifestation of tumor spread into fat, but compared with corresponding histology sections, this represents perivascular cuffing and peritumoral spicules of connective tissue that do not contain tumor. Irregularity of the bowel wall is also limited as a diagnostic criterion as this frequently correlates with normal bowel contour made irregular by sometimes incomplete bands of longitudinal muscle. This criterion has also been shown to be unreliable by Schnall et al. [30].

When colorectal adenocarcinomas encompass the full circumference of the bowel wall, they produce marked narrowing of the bowel lumen increasing the risk of bowel obstruction or perforation (Fig. 10). Tumors may ulcerate despite being relatively small. The ulcerating structure may also produce stenosis. Central ulceration of tumor causes focal thinning and structuring of the bowel wall. In some cases severe ulceration by the tumor causes more diffuse thinning of the bowel so that the bowel layers are no longer discernible. Ulcerating tumors are the most difficult to delineate on MR images [7], showing little or no tumor bulk but conversely demonstrate thinning of the bowel wall layers making individual layers difficult to differentiate. For this reason the degree of extramural spread is poorly depicted [7].

Polypoidal tumors

Exophytic or polypoidal tumors have a protuberant appearance with the tumor mass projecting into the lumen. A number of studies have observed that such polypoidal lesions are often of a relatively low grade of malignancy despite their obstructing intraluminal mass lesions [35–37]. Early tumors developing within benign polypoidal adenomas usually become pedunculated, and are broken into lobules with intercommunicating clefts resulting in a characteristic papillary surface. One such form is the villous adenocarcinoma, which presents typically as a protuberant soft and often friable sessile mass with a shaggy or velvety surface. Such tumors can attain a

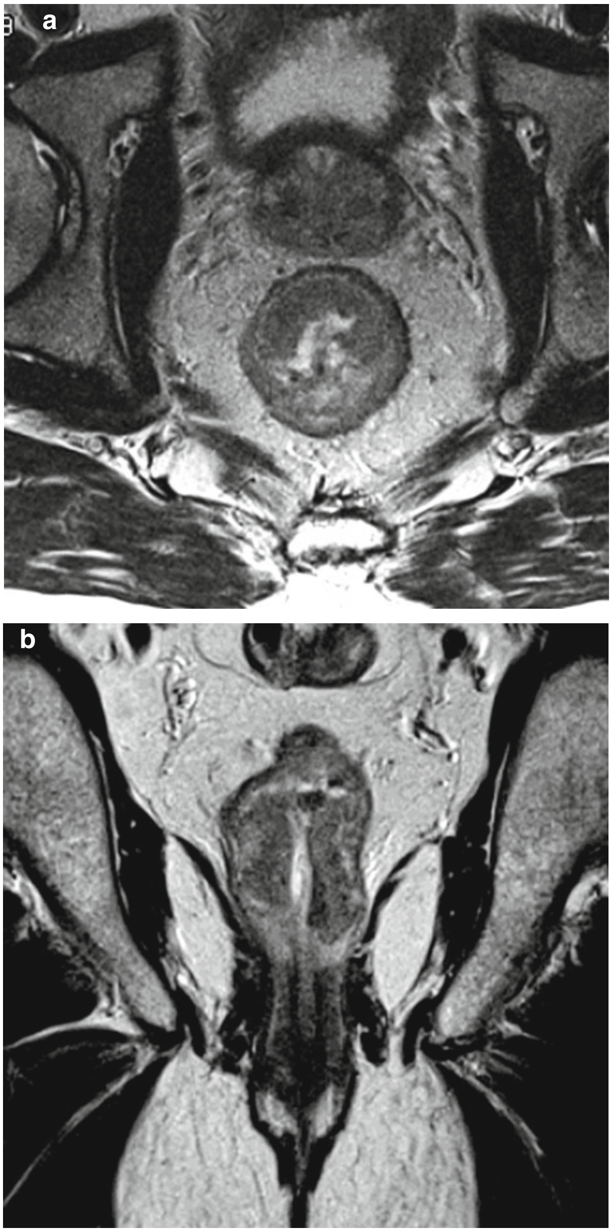

Fig. 10. Circular stenosing tumor of the lower rectum in axial (**a**) and coronal (**b**) views

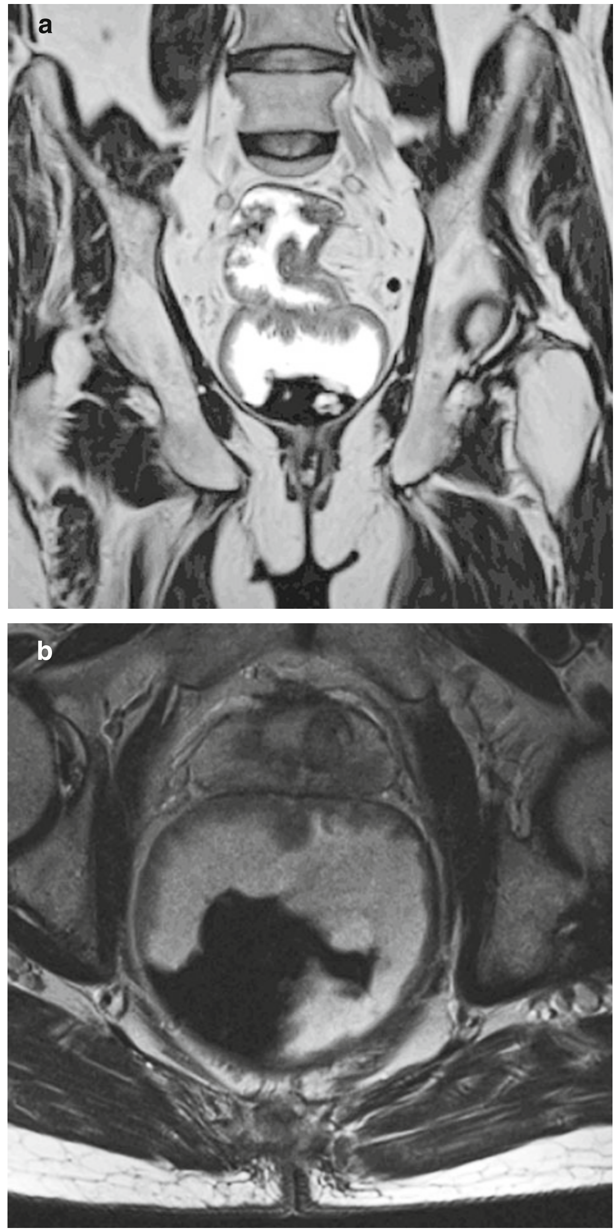

Fig. 11. Coronal (**a**) and axial (**b**) images of a mucinous carcinoma. The mucin is shown as fluid-intense material filling the lumen of the rectum completely

large size with only minimal infiltration of the bowel wall. On MRI, these tumors frequently show clefts containing high signal corresponding to mucous fluid on the papillary tumor surface [7].

Mucinous tumors

Mucinous tumor sare an own morphological subgroup. They account for about 10% of carcinomas of the colon and show worse prognosis compared to other subgroups. A number of authors have observed the association between mucinous carcinoma and poor prognosis [38, 39] which is thought to relate to the fact that these tumors have a poorly defined advancing margin and are often very advanced at presentation [40]. They are also thought to infiltrate diffusely and unlike non-mucinous tumors, they can spread intramurally. On MRI, these tumors are of very high signal intensity (same signal as water). The bowel sometimes shows expansion by high signal intensity (Fig. 11). They also can present as a cystic mass perirectally because of their ability to penetrate the rectal wall.

Differentiation of mucinous tumors and high signal intensity areas in other types can be difficult (Kim et al. 2003 [41]) the use of Gd-enhanced T1-weighted sequences may improve differentiation. The mucin pool can show enhancement as reported by Hussain [42].

Staging of rectal tumors

Image interpretation criteria for T staging

The patterns of tumor spread on MRI have been evaluated and correlated with histologic specimen. Typical MRI appearance has been described and published [7].

Intermediate signal intensity within the mucosa and submucosa with preservation of a thin layer of submucosa deep to "tumor" signal corresponds to tumor confined to the submucosa (pT1) tumor. When tumor signal extends into the circular muscle coat but does not extend through the full thickness of muscle, this corresponds to histological pT2. Replacement of the whole muscular layer by intermediate signal intensity, can correspond to pT2 or pT3 tumor. It is often not possible to distinguish between the two (Fig. 12).

A broad-based zone of intermediate signal intensity extending into perirectal or pericolonic fat corresponds to tumor stage pT3. An irregular bowel contour has been shown on histologic samples to be caused by the corrugated muscle layers of the bowel wall.

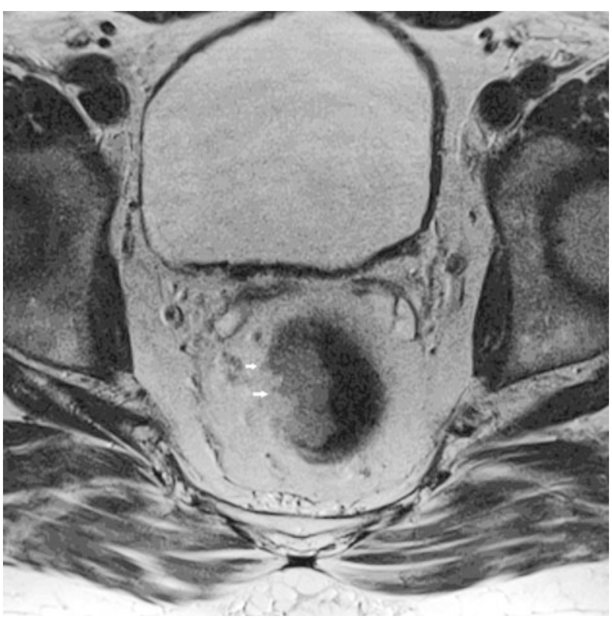

Fig. 12. Axial T2 weighted images of a polypoid rectal tumor showing spicular margins protruding into the mesorectal fat. The tumor proved to be stage pT2 on operation

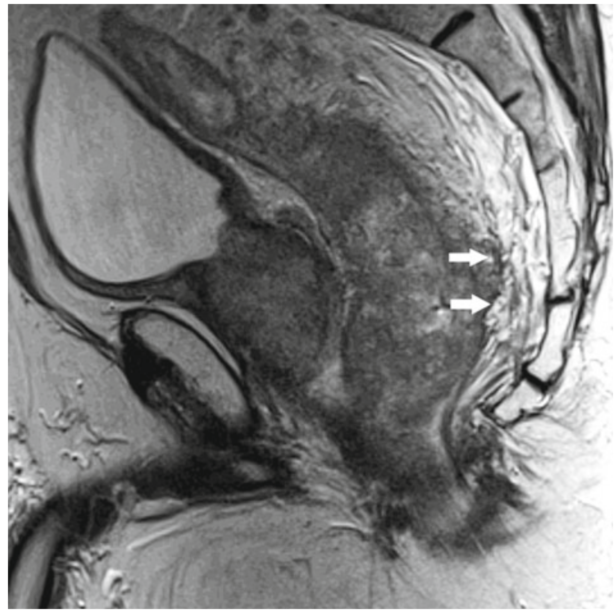

Fig. 13. Sagittal T2 weighted Image. Large rectal carcinoma. This stage T3 tumor shows broad infiltration of the mesorectal fat (arrows), nearly reaching the dorsal mesorectal fascia

Low signal intensity spiculation from the bowel wall into adjacent fat can correspond to perivascular cuffing of connective tissue or peritumoral desmoplastic response. It is a very unreliable feature of T3 spread. A number of authors have shown a relationship between poor survival and increasing depth of extramural spread that is independent of other prognostic factors including the circumferential margin status [43, 44]. Although the accuracy of preoperative staging techniques is limited by overstaging or understaging of borderline T3/T2 tumors, there is rather limited importance in differentiating between minimal T3 infiltration and T2 lesions since both have favorable survival and are thus unlikely to obtain benefit from adjuvant therapy unless the potential circumferential margin is threatened [45, 46]. On the other hand it is important to reliably identify tumors with increasing extramural spread as histopathology studies have shown poor survival in this group of patients (Fig. 13). Brown et al. showed that the majority of patients with tumor infiltrating 5 mm or more beyond the muscularis propria are correctly identified, and extramural depth, as measured using MRI, shows direct agreement with corresponding histopathological measurements [45, 46].

Lymph node staging

The presence of tumor containing lymph nodes close to the surgical resection margin increases the risk of recurrence [47]. In Europe patients with nodal disease outside the mesorectal fascia in rectal cancers do not routinely undergo pelvic sidewall dissection and preoperative therapy is usually given instead [48]. The ability to determine reliably node-negative status preoperatively could result in less aggressive surgery and preoperative therapy in some patients. At present preoperative imaging cannot reliably exclude microscopic nodal involvement. Several authors propose, that the decision to treat using local excision should be based on histological assessment of the depth of tumor invasion [49, 50]. Dworak showed considerable size overlap between normal or reactive nodes and those containing metastases [51]. He found that the only positive lymph nodes in 31 out of 98 rectal cancer patients measured <5 mm. Schnall et al., using endorectal MR, noted that positive lymph nodes varied substantially in size, with 5 out of 12 nodes measuring 5 mm or less containing tumor [30].

With all different cut off sizes, the overall predictive value of MR size was poor because of substantial overlap in size between nodes that are benign and malignant. Brown et al. [52] showed in a study in which 437 nodes in 42 patients where characterized according to their border contour and signal intensity, that these criteria improved the specificity of Lymph node staging (Fig. 14). Although the ability of MRI to resolve nodes <3 mm in diameter is suboptimal, it seems that MR evaluation of nodes using these morphological criteria will result in understaging of very few patients. In cases of image degradation owing to patient movement or if there is a poor signal to noise ratio, confident assessment of nodal status will be limited.

Venous spread

Extramural vascular invasion is known as an independent predictor of local and distant recurrence and poorer overall survival an was reported to occur in up to 52% of cases of rectal cancer [5, 8–10 Smith]. Talbot and Ritchie (1980) [53] published a histological analysis of 703 rectal cancer surgical specimens. They observed that the presence of invasion of extramural veins by tumor was associated with a low 5-year survival rate (33%), and was an important prognostic factor associated with a much lower survival regardless of Dukes stage. In different studies following, the presence of venous invasion was correlated with survival and the pattern of treatment failure [54, 55]. By correlation with histopathology high-resolution MRI was shown to identify extramural vascular invasion (EMVI) preoperatively [45] (Fig. 15). Patients diagnosed with MRI-EMVI positive tumors have a significantly worse outcome with an overall risk of developing distant metastases (either synchronous or delayed) greater than 50%, compared with only 12% for patients who are MRI-EMVI negative. Extramural venous invasion is recognized on MRI by characteristic serpiginous extension of tumor signal into perirectal or pericolonic fat [45]. Smith et al. [56] have described the invasion of tumor into vessel as intravascular presence of tumor signal. The vessels may become expanded and if the tumor expands through the vessel wall, the vessel border may become disrupted, resulting in either irregular or nodular appearance.

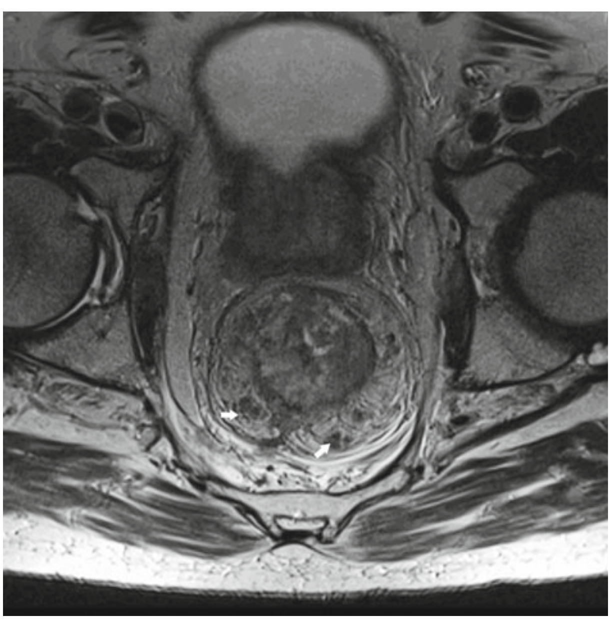

Fig. 14. Tumorous mesorectal lymph nodes with low signal intensity and irregular borders (arrows)

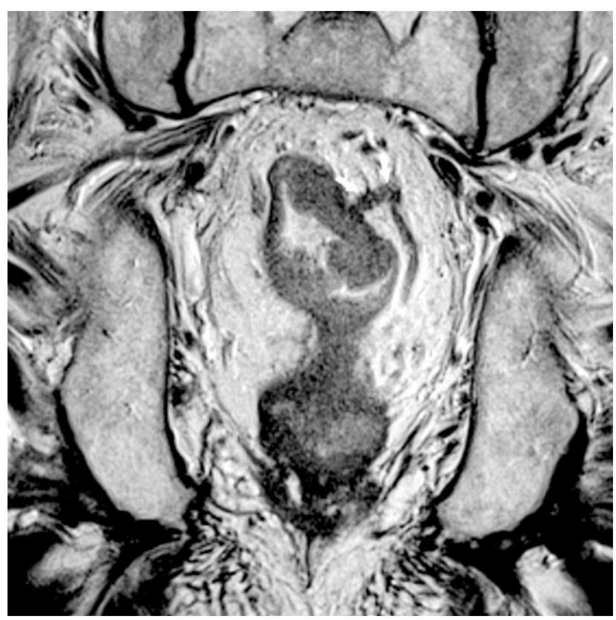

Fig. 15. Coronal image of large rectal cancer showing venous invasion on the right (arrow) note the longitudinal spread along the vessel into the perirectal fat

According to imaging criteria (tumor margin, tumor location relative to vessels, vessel size and vessel border) a 5-point grading system for MRI-based preoperative assessment of extramural vascular involvement has been proposed [45, 56].

The circumferential resection margin in rectal cancer

Incomplete removal of the lateral extension of the tumor is a main source of local recurrence [47, 57]. The mesorectal fascia represents the potential CRM and its clear demonstration on MRI enables prediction of final CRM status in patients undergoing TME surgery. Hall et al. [58] prospectively studied outcome in patients with positive circumferential margins. In contrast to the group's earlier studies positive CRM did not predict local recurrence but did influence overall disease-free interval and survival rates. It was postulated therefore that CRM positive status following TME surgery might either reflect poor surgical clearance or advanced disease that cannot be influenced by surgery. In a setting of neoadjuvant therapy, the regression of margin involvement is of prognostic importance. Natgegaal and Quirke (2008) showed that if the margins remain positive, prognosis is even worse than in cases without therapy because of resistant tumor cells [59].

MRI provides accurate information on CRM [45]. Beets-Tan et al. [6] found that the distance to the mesorectal resection plane can reliably be shown by MRI with phased array coils. A tumor free margin of 1 mm can be predicted with high certainty, if the measured distance in MRI is at least 5 mm. MRI is more reliable in predicting tumor free margins as for T-staging. Combined with N-status, CRM status as shown on MRI examination provides a better prognostic model as the TNM system [60, 61]. Margin involvement can be described by either direct or discontinuous tumor spread, venous or lymphatic invasion, lymph node metastases or perineural tumor spread [62, 63].

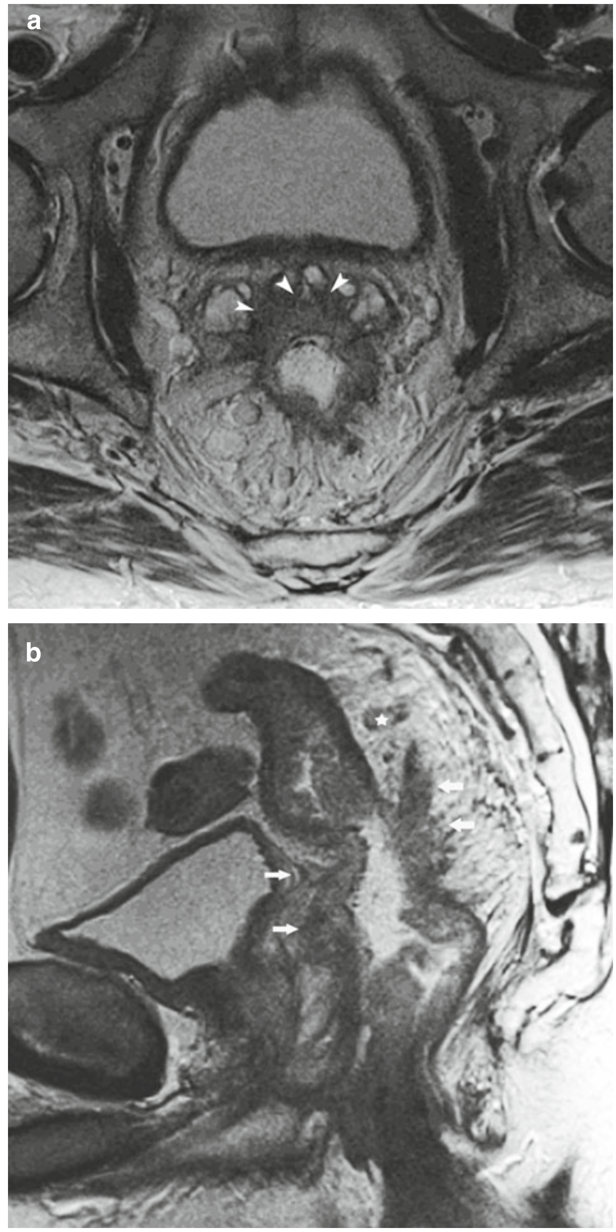

Fig. 16. Axial T2-weighted image (**a**) showing a stage T4 tumor with invasion of the seminal vesicles (arrowheads). In the sagittal plane (**b**) infiltration of the seminal vesicles and prostate as well as extensive speculated invasion of the dorsal mesorectal fat can be recognized (arrows). Enlarged mesorectal lymph node (asterix)

Sphincter infiltration

A greater number of positive resection margins can be found in the lower rectum (Fig. 16). The radiologic prediction of tumor free margins is far more difficult in this tumor location but is of utmost importance in choosing the appropriate treatment. This is especially true for prediction of involvement of the anal sphincter complex. In a series of 61 patients Urban et al. [13] proved that MRI was able to predict sphincter infiltration with high sensitivity and specificity. Holzer et al. [12] showed the excellent correlation between preoperative MRI and histological findings in patients treated with intersphincteric resection. Infiltration of the sphincter apparatus occurred only in tumors extending into the anal canal, infiltration of the external sphincter was present only in 5% of the cases of sphincter infiltrating tumors, all others (28%) were confined to the internal sphincter (Figs. 17–19). In these studies T1 weighted imaging with administration of Gd was used, which still shows superiority even to high resolution T2 weighted sequences in selected cases for

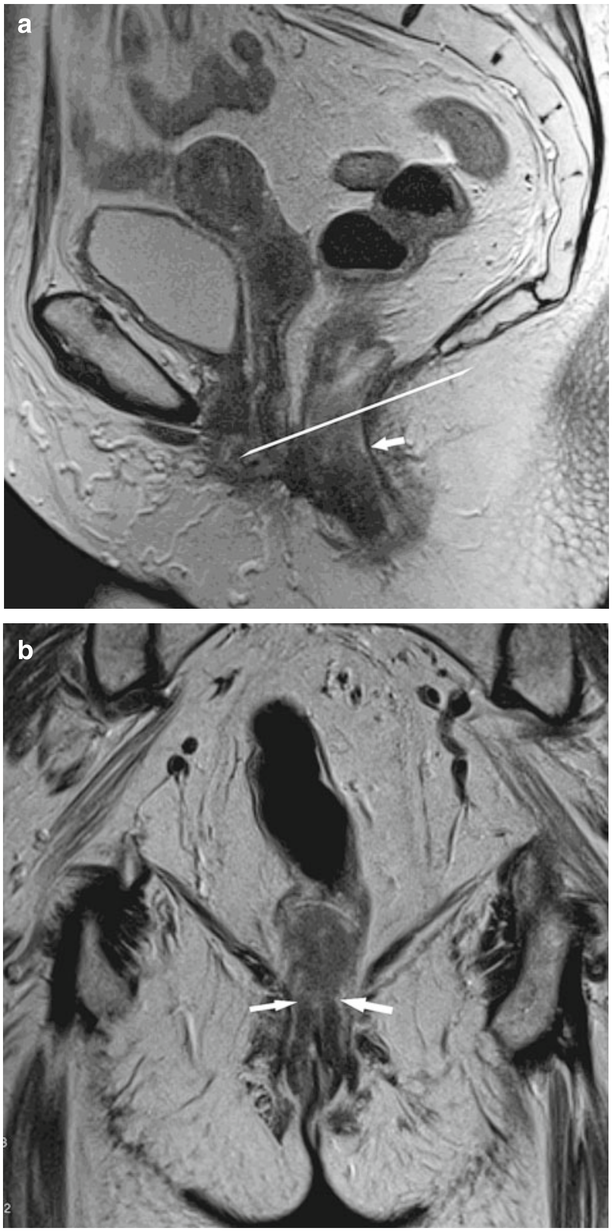

Fig. 17. Sagittal (**a**) and coronal (**b**) images of low rectal cancer. Tumor growing to the oral end of the anal canal without infiltration of the sphincters (arrows)

Fig. 18. Tumor infiltration of the internal sphincter is shown on coronal T2-weighted images (arrows). Note the intact external sphincter

Fig. 19. T4 rectal cancer invading the internal and external sphincters on the left side, growing out into the ischiorectal fossa shown on this coronal T2-weighted image

differentiation of tumor margins and the anal sphincters in those low and ultralow lying tumors.

Future developments

Moving table MRI

Whole Body MRI today is considered a diagnostic procedure capable of determining the extent of metastatic spread. New techniques of imaging with moving MRI-tables have made it possible to acquire data at a number of successive stations with the table at rest step by step [64]. There is now a different approach based on data collection during continuous table movement [65–68]. With this technique, patient repositioning and stepwise whole body examination are no longer needed. Imaging can be performed similarly to standard helical CT. This has lead to a dramatic improvement in diagnosis [69, 70].

Diffusion weighted imaging

Diffusion weighted imaging (DWI) explores the random motion of water molecules in the extra- and intracellular spaces ant intravascular space. This provides qualitative and quantitiative information about tissue cellularity and cell membrane integrity [71]. Different technical approaches are used for whole body diffusion weighted imaging with suppression of background body signal [72]. Apparent diffusion coefficient (ADC) measurements appear to be predictive of tumor response to chemotherapy and radiation. Studies in rectal cancer have shown that tumors with low pre-treatment ADC (highly cellular tumors) respond better to adjuvant treatment compared to tumors with high ADC values [73, 74]. A possible explanation is that the latter are likely to be more necrotic and poorly perfused, leading to reduced sensibility to adjuvant measures [71].

MRI after neoadjuvant therapy

The aim of neoadjuvant chemotherapy or chemoradiation is to make complete tumor resection possible even in advanced cases (Fig. 20). These therapies lead to downstaging of the tumor and up to 20% of patients even show complete tumor regression [75–78]. The Swedish rectal cancer trial [79] showed, that a short cycle of preoperative radiotherapy reduces the local recurrence rate to 11%. Another study proved, that even patients who underwent TME which has lower recurrence rates than other surgical methods benefit from preoperative radiation [80]. Vliegen et al. (2008) evaluated the value of MRI after chemoradiation for the prediction of tumor invasion of the mesorectal fascia [81]. The main difficulty they found in this study was the assessment of diffuse fibrotic tissue in the initial tumor area which is seen in 50% of the patients. Residual tumor in these fibrotic areas is often confined to small nests of tumor cells that cannot be discriminated with MRI [82, 83]. Despite this problem, some potentially helpful morphologic patterns can be found. The presence of iso or hyperintense tissue infiltration of the mesorectal fascia is associated with tumor invasion at histologic examination in 90% of the quadrants where these changes can be seen [80]. Allen et al. (2007) found that 63% of tumors shrank after chemoradiation so that a partial response could be postulated. Only 17% showed downstaging of the tumor. Nodal downstaging occurred in 68% of the cases. MRI in this study was only of moderate accuracy in patients with rectal cancer that had undergone long-course preoperative chemoradiation. The residual high signal intensity in mucinous tumors proved to be incorrectly diagnosed as tumor, histologic examination showed only mucin lakes in many cases [84].

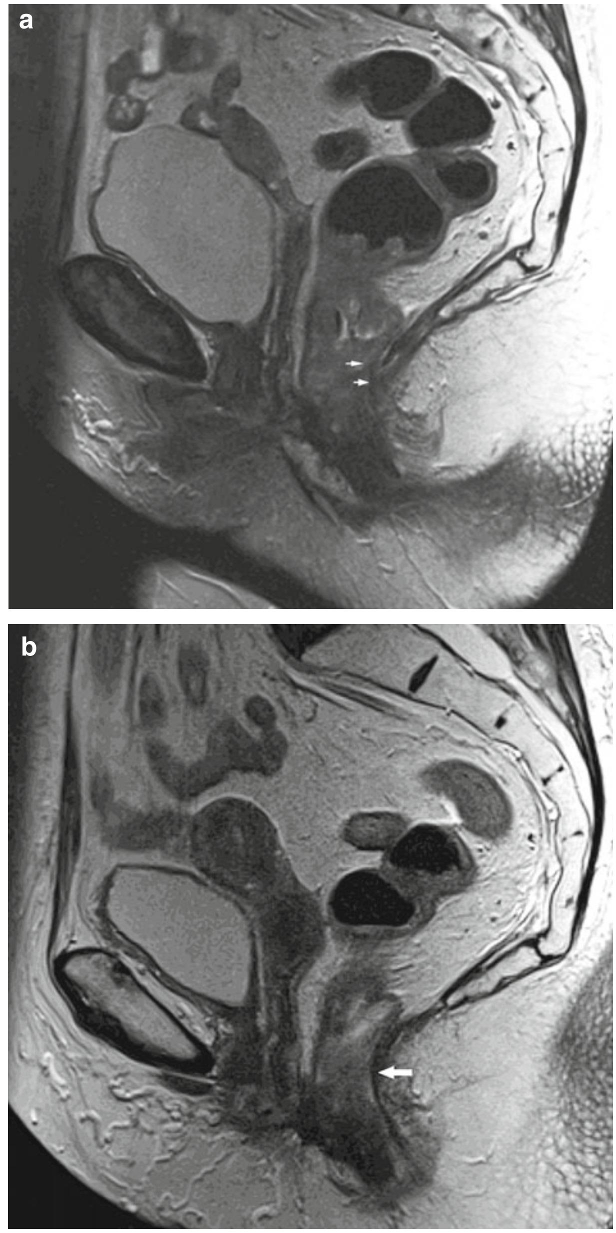

Fig. 20. Sagittal images before (**a**) and after (**b**) chemoradiation therapy in a patient with a large tumor of the low rectum. The tumor cannot be separated from the pelvic floor dorsally in the first examination (arrows in a). Shrinkage of the tumor with clear delineation of the pelvic floor structures and hyperintensity of the residual tumor after neoadjuvant therapy

Short course radiation therapy 1 week prior to surgery resulted in no histopathologically discernible effect. There was particularly no inflammatory reaction or fibrosis [85]. After long-course chemoradiation, reliable differentiation between active tumor and fibrosis is not possible, Koh et al. (2005) showed an overall staging accuracy of only 47% [9]. On the other hand CRM regression was frequently found. The distance between tumor and CRM was accurately predicted. Chen et al. (2005) reported an overall accuracy for T-stage after neoadjuvant chemotherapy of 52%, overstaging occurred in 38%, understaging in 10% of cases [86]. While Peschaud et al. (2005) showed correct prediction of CRM involvement in 70% of patients, this was only the case in 22% of the patients with cancer of the low rectum [87].

Conclusion

MRI with the use of phased array coils has shown to provide excellent visualisation of the important pelvic structures and spatial distribution of rectal cancer. High resolution MRI allows to predict CRM status and extramural tumor spread. In the MERCURY-study it has been proved that a standardized examination and reporting protocol leads to reproducible and accurate results in a multi center setting. Low and ultra-low rectal tumors require special staging measures due to the anatomic situation with tapering of the mesorectum and different new sphincter-preserving operation methods. A tailored imaging approach for each case may be necessary besides standard MR-sequences in order to enable the radiologist to provide the surgeon with precise information on the relation of the tumor to the structures of the pelvic floor and sphincter apparatus. Changes after neoadjuvant chemotherapy or radiation have to be evaluated carefully. New imaging techniques as diffusion weighted MR imaging or PET have to be evaluated on their ability to discriminate active tumor for post-therapy changes.

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Preoperative therapeutic options

Selective non-operative management of distal rectal cancer: The Watch & Wait Protocol

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Rationale for a non-immediate surgical approach

The observation of improved local disease control with the use of preoperative chemoradiation (CRT) for locally advanced rectal cancer established this treatment strategy as one the preferred initial approaches for this disease. Interestingly, the benefits of preoperative CRT were not restricted to local recurrence rates but also included reduced toxicity rates compared to postoperative CRT, significant tumor downstaging and downsizing, greater rates of sphincter preservation, and better functional results [1, 2].

In some cases tumor regression was so significant, that no residual cancer could be detected in the pathological specimen, a phenomenon known as complete pathological response (pCR).

Even though radical surgery (with TME) is still a cornerstone in the treatment of rectal cancer, it is associated with significant immediate morbidity and mortality. Anastomotic leak is probably the most important complication and is reported in up to 12% of cases [2, 3]. Perioperative mortality may reach 3% and is significantly higher, reaching up to 13% when an anastomotic leak is present among patients who do not undergo temporary diversion [4, 5]. Considering the fact that temporary stoma is almost always required, additional morbidity or even mortality related to stoma creation and take-down should be considered in the cumulative morbidity of rectal cancer management [6]. Also, even though nerve-preserving technique is now standard, the rates of urinary and sexual dysfunctions are quite significant. Finally, even though sphincteric function and quality of life among patients undergoing ultra-low anterior resections are acceptable, results are far from perfect. In a recent report of patients undergoing ultra-low anterior resections, the median fecal incontinence score rate was 11 with nearly half of patients with significant fecal incontinence [7].

In addition, final pathologic disease stage (after CRT) is the most significant prognostic factor in patients with rectal cancer [8]. Patients that develop complete tumor regression (pCR) seem to be associated with improved oncological outcomes [9]. In this setting, it seems appropriate that those patients with no residual cancer, that are associated with the best oncological outcomes would benefit the most from avoiding radical surgery and its associated morbidity and mortality rates.

The question that emerges is: *Is it justified to make our patients undergo a morbid and sometimes mutilating procedure when not even a single cancer cell is collected?* In this setting, identification of patients with complete tumor regression determined by clinical, endoscopic and radiological assessment has been proposed in order to avoid immediate TME in a significant proportion of patients at high risk for developing pCR.

More than providing a radical change in the management of rectal cancer, this approach consists of close surveillance of a select group of patients with a high suspicion of complete tumor response without immediate radical surgery. In one hand, patients with no residual cancer may have a chance to be spared from a major surgical procedure while on the other hand, patients with minimal residual disease and suspected for complete response will have surgery slightly postponed or delayed without any oncological compromise.

Response assessment

In order for such an approach to be feasible, tumor response assessment must be accurate and efficient. Unfortunately, there is still no perfect and definitive tool for this purpose. Instead, a combination of different modalities may be useful in identifying those patients more likely to harbor no residual cancer. Considering very stringent criteria of these different modalities, such patients have been considered complete clinical responders (cCR).

Clinical assessment

Residual symptoms after CRT should be considered with caution as indicator of a complete response. Even though they may subside in patients with cCR, most patients will present symptom relief despite the presence of residual cancer.

However, clinical assessment including digital rectal examination and proctoscopy by an experienced colorectal surgeon is definitely one of the most important tools in assessment of tumor response. Even though studies have reported disappointing results regarding sensitivity and specificity of this modality in identifying pCR patients, a few considerations may be worthwhile mentioning. First, standardization of what a complete clinical response was and is still unavailable. Also, patients were assessed in these studies using rather short intervals from CRT, a well-known factor that may considerably affect response rates. Finally, the fact that examinations were performed by different surgeons with different experiences, could also have influenced results [10].

In an effort to provide unification and standardization of clinical and endoscopic findings among patients with complete clinical response, our group has recently reported commonly observed features among these patients as well as findings that should warrant prompt surgical action. Not only these findings may aid surgeons in identifying individual patients that are likely to present complete tumor regression, they also may provide a basis for standardization of cCR in order to allow future clinical trials interested in investigating the role of alternative treatment strategies in such patients [11].

According to the stringent criteria provided in that report, patients with the following findings at digital rectal examination and proctoscopy (that can be performed either using rigid or flexible scopes) may be considered as complete clinical responders:

1. Whitening of the mucosa in an area of the rectal wall may be frequently observed in patients with cCR (Fig. 1).
2. Teleangiectasia (small derogative blood vessels seen on the rectal mucosa at the area previously harboring the primary cancer) is also frequently observed in complete clinical responders, even in long-term follow-up.
3. A subtle loss of pliability of the rectal wall harboring the scar; usually observed during manual insufflations at proctoscopy with light stiffness of the wall. In the context of no additional positive findings of residual cancer, this may also be considered as a feature of cCR
4. Whenever a tumor cannot be felt or seen, patients should be considered as complete clinical responders.

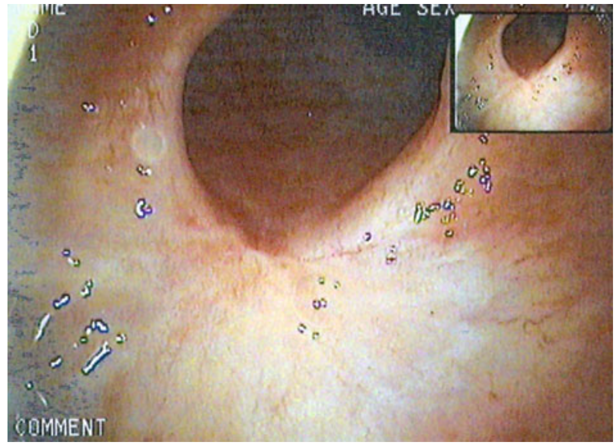

Fig. 1. Endoscopic view of a patient with Clinical Complete Response

Alternatively, the following findings should be considered as incomplete clinical response and therefore warrant immediate surgical action. Even though this may lead to a proportion of patients with pCR despite clinical findings of persistent cancer, it seems to be the safest procedure.

1. Any residual deep ulceration with or without a necrotic center.
2. Any superficial ulcer, irregularity, even in the presence of only mucosal ulceration.
3. Any palpable nodule, easily defined by digital rectal examination, even in the presence of mucosal complete integrity.

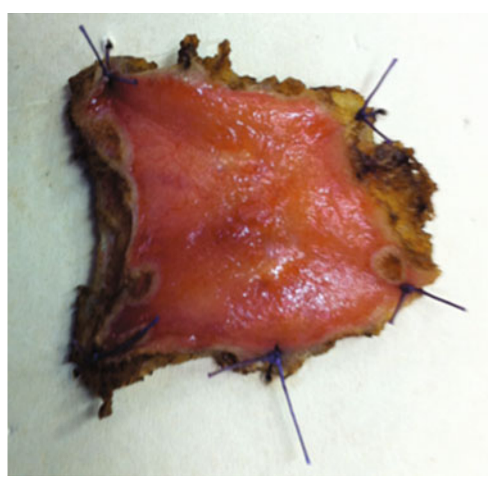

Fig. 2. Surgical specimen of a patient with significant tumor downsizing operated by transanal endoscopic microsurgery (TEM)

These endoscopic and clinical findings should be considered of great risk for the presence of residual cancer. In any of these situations, a surgical action is warranted, at least for diagnostic purposes. A non-surgical approach in this scenario is not recommended (Fig. 2).

Radiological studies

Magnetic Resonance Imaging (MRI) and Endorectal Ultrasound provide appropriate primary staging of rectal cancer. Information on T-level classification and distance of the tumor to the mesorectal fascia correlate well with final pathological findings of these patients. Nodal staging is less accurate irrespective of staging modality.

However, after CRT, accuracy of T-level classification has been disappointing and in the range of 50% [12, 13]. If nodal staging seems rather inaccurate even without neoadjuvant CRT, after such treatment, precision may be even worse. Even highly experienced radiologists seem to be better off distinguishing tumors that are restricted to the rectal wall (ypT0-2N0) from those that penetrate through the wall or harbor lymph node metastases (ypT3 or ypN+) instead of providing exact post CRT ycT and ycN staging.

Rectal tumor volumetry on standard T2-weighted MR images was studied by some authors for the assessment of response after CRT with conflicting results. One report did not find difference in tumor volume reduction rates between patients with pCR and those with residual cancer [14]. Confronting this result, a more recent report found that a tumor volume reduction rate of more than 75% was associated with the development of pCR [15].

The introduction of diffusion-weighted (DW) MRI has attracted new interest on the matter. A recent multicentric study, reviewed 120 patients by three trained radiologists comparing standard MRI with DW MRI. Surprisingly, all of them found improvement in sensitivity and specificity rates for the detection of pCR [16]. This imaging modality was able to accurately predict pCR in 94% of the cases. Another recent report showed that post-CRT volumetry on DW-MR images were significantly more accurate than on T2-weighted MR images to assess a CR after CRT [17]. Although promising, more evidence is needed before these tools could be incorporated into routine clinical practice.

In our practice, MRI and/or endorectal ultrasound (ERUS) probably are best suited for the diagnosis of residual extrarectal disease, such as a mesorectal enlarged nodes or masses than for the diagnosis of a cCR. The presence of some thickening of the rectal wall, presence of small perirectal nodes (less than 5 mm) or densification of the perirectal fat, should not prompt any specific or

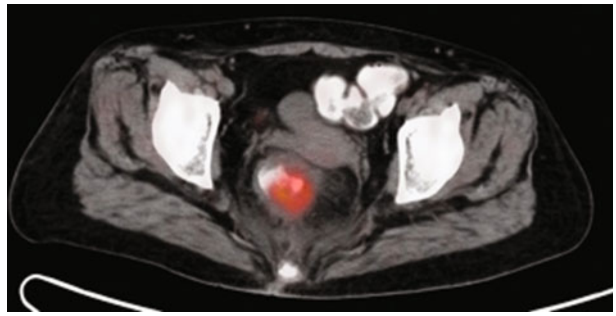

Fig. 3. 12 week PET/CT Scan of a rectal cancer patient treated with neoadjuvant chemoradiation. Metabolic active lesion at rectal wall suggesting incomplete response to therapy

immediate surgical attention, particularly when endoscopic and clinical assessment are normal. These findings are commonly seen in patients with cCR. Alternatively, the presence of highly suspicious perirectal nodes should prompt radical resection. Even though the presence of residual metastatic nodes in the setting of complete tumor regression (ypT0N+) is not frequent, it has been reported in up to 7% of the cases.

Many expectations have been put in PET/CT in this setting since it provides metabolic information of a given tumor in addition to the structural anatomical findings. This study also provides an objective parameter of tumor metabolic activity by the maximum *Standard Uptake Value* (SUVmax), that can be measured (Fig. 3).

One study of 25 patients with rectal cancer compared the results of baseline PET-CT with a second PET-CT performed after 6 weeks from CRT completion. All patients included in the study experienced a decrease in maximum standard uptake values (SUVmax) between baseline and 6-week PET-CT scans. Also, the final SUVmax obtained at 6 weeks was significantly associated with primary tumor downstaging (patients with tumor downstaging exhibited significantly lower SUVmax) [18]. In another study from Memorial Sloan Kettering Cancer Center including 15 patients undergoing baseline PET followed by a second PET 6 weeks after CRT completion, a visual response score was shown to provide superior prediction of tumor downstaging in addition of the extent of pathologic response to CRT compared to standard CT [19].

These results although promising, should be carefully evaluated since only a small number of patients were included and as will be discussed later, the tumor response was assessed rather shortly (6 weeks) after CRT completion. In another study, 30 patients with locally advanced rectal cancer treated with CRT and surgery were assessed by pre and post-CRT PET-CT for tumor response after 7 weeks from CRT. PET/CT correctly identified six of eight patients with pCR (specificity 75%); unfortunately sensitivity was only 45 percent and accuracy 53 percent. The positive and negative predictive values were 83 and 33 percent, respectively. The authors concluded that PET/CT could not predict the pathological response in locally advanced rectal cancer [20].

More recently, we were able to conclude a prospective study using PET/CT for the detection of complete tumor regression (pCR or cCR) in considerably larger sample size. After including 99 patients, PET/CT at 12 weeks from CRT completion was able to detect residual cancer with an overall accuracy of 85% and significantly better specificity and sensitvity rates. Even though assessment with PET/CT alone was not superior to clinical assessment alone (accuracy of 91%), it could have potentially corrected "mistakes" made by clinical assessment improving overall accuracy to 96% [21].

CEA

Determination of CEA levels before and after CRT may be useful during assessment of tumor response. In one study with over 500 patients undergoing neoadjuvant CRT, low baseline (before CRT) CEA levels were significant predictors of ypCR after radical surgery in univariate analysis [25]. Curiously, another retrospective report of patients undergoing different CRT regimens showed that a pre treatment CEA level <2.5 ng/dl was predictor of ypCR [22].

An increase in CEA levels or persistence of at least 70% from baseline levels has also been suggested as a significant predictor of worse outcome in patients with CEA levels >6 ng/ml at baseline [23]. Also, different cutoff values have been considered for patients undergoing CRT when compared to standard colorectal cancer patients. A retrospective analysis of 109 patients undergoing neoadjuvant therapy, identified a cutoff value for CEA <2.7 ng/ml at 4 weeks from RT completion to be a statistically significant and independent predictor of tumor regression [24].

Among our own series of patients undergoing, we found no correlation with both pre-treatment CEA and variation between pre and post treatment CEA levels with tumor response and oncological outcomes. On the other hand, a post CRT level <5 ng/ml after at least 8 weeks from CRT completion was a favorable prognostic factor for rectal cancer associated with increased rates of earlier disease staging and complete tumor regression [25].

Endoscopic biopsies after CRT

During endoscopic evaluation of a residual lesion, forcep's biopsies are frequently performed and considered by many to be useful in assessement of tumor response. Even though a positive result implies obvious persistence of residual tumor, negative results may warrant cautious interpretation.

In a retrospective review of patients undergoing post-CRT biopsies, the negative predictive value was as low as 36% [26]. However, it should be noted that these were unselected patients being assessed significantly earlier than 8 weeks from CRT completion.

In a retrospective review of patients undergoing neoadjuvant CRT restricted to patients with significant tumor downsizing, and therefore who were at increased risk to have possibly developed pCR, post-CRT biopsies resulted in a negative predictive value of 21% [27]. In this setting, a negative biopsy of a clinically detectable lesion, even after significant tumor downsizing was not useful for ruling out residual disease and should not prevent surgeons from performing surgical resection. In select cases, excisional biopsy (through a full-thickness local excision) may be considered either as a diagnostic or therapeutic procedure for definitive information on tumor response to CRT.

Factors associated with tumor response after CRT

Tumor response to CRT is not uniform and many factors may play a role. CRT regimen as well as time for assessment of response appear to be as important as tumor and patient characteristics. In this section, the most significant factors are reviewed.

Chemoradiation regimen

Fractionated long course chemoradiation followed by surgery after 6–8 weeks or pelvic short-course irradiation with 25 Gy in five fractions followed by immediate surgery (short-course) are the two most used regimens in the preoperative treatment of patients with resectable T3-4 rectal cancer. Benefits in local disease control seem to be equivalent between them, but there are significant differences in terms of tumor downstaging [28].

The rates of pCR are significantly lower in patients undergoing short-course RT, when compared with those undergoing long-course. At first glance, the long-course regimen includes chemotherapy and this could be determinant for that difference. It should also be considered that damaged cancer cells need time to undergo necrosis after radiotherapy and usually patients undergoing short-course RT, surgery is performed 1 week after RT completion whereas long-course CRT is followed by radical surgery after at least 6–8 weeks.

Indeed, the addition of chemotherapy has been shown to improve rates of tumor downstaging as well as local disease control (i.e. lower recurrence rates) [29, 30]. In a randomized trial of patients undergoing RT with or without 5-FU– based chemotherapy, patients in the CRT group more frequently had a complete pathologic responses less lymph node metastases as well as vascular invasion. Additionally, patients treated by CRT had fewer overall lymph nodes recovered in the resected specimens and decreased tumor size [29].

A review of phase II and III studies using different neoadjuvant CRT regimens for rectal cancer identified several predictive factors for complete pathologic response, including the dose of radiation therapy delivered, the method of 5-FU infusion, and the use of additional drugs to standard 5-FU based regimens. After reviewing over 4000 patients in 71 studies treated with different regimens, complete pathologic response ranged from 0% to 42% and was significantly associated with the delivery of radiation doses higher than 45-Gy, 5-FU regimens with continous infusion, and the use of a second drug, most frequently oxaliplatin [31].

The association of higher rates of pCR and the addition oxaliplatin to the traditional scheme of 5-FU has been strongly questioned in light of the results of a recent prospective randomized trial that showed that this addition was not associated with better rates of pCR. Moreover, patients treated with oxaliplatin experienced significantly more treatment-related toxicities [32].

Targeted biological drugs used for metastatic disease, such as bevazicumab and cetuximab, were included in phase I and II protocols in combination with other drugs with the hope of increasing response rates. However, these expectations were not fulfilled in any of the studies among patients undergoing this ‘triple’ therapy (5-FU, oxaliplatin, and cetuximab). A review of these trials also suggested a subadditive interaction between capecitabine, oxaliplatin, and cetuximab as reflected by decreased rate of pCR (9 *vs.* 16%) and significant decrease in tumor regression grades (more than 50% of tumor regression) among surgical specimens from these patients when compared with patients undergoing treatment with capecitabine and oxaliplatin alone CRT regimens [33]. It is not clear whether the inclusion of patients according to the K-ras status could have any influence in response to neoadjuvant CRT with this triple approach [34].

Time for tumor response assessment

The Lyon Trial randomized 201 patients with distal rectal cancer T2-3Nx before radiotherapy (39 Gy in 13 fractions) into two groups. The short interval group had surgery performed within 2 weeks after completion of radiation therapy compared to 6 weeks in the long interval group. After a median follow-up of 33 months, no differences in local relapse, morbidity and short-term survival between the two groups could be observed. On the other hand, improved clinical tumor responses ($p = 0.007$) and pathologic downstaging (10.3% *vs.* 26% $P = 0.005$) were observed in the long interval group [35]. These results provided the only prospective evidence, up to present day, to support an interval period of at least 6 weeks from CRT completion before surgery in order to obtain maximal or optimal tumor downstaging.

Recent retrospective studies were able to provide evidence that longer periods after CRT completion could be associated with higher rates of tumor downstaging. These studies have shown that patients managed by radical surgery 7 to 8 weeks after CRT completion had increased rates of complete pathological responses [36, 37]. In another retrospective review from the Cleveland Clinic of patients managed by neoadjuvant CRT, a steep increase in complete pathological response rates was observed when surgery was performed after 7 weeks from CRT. Also, the rates of complete response seem to stabilize only after 12 weeks, suggesting no additional benefit in terms of tumor downstaging after this time [38]. Another study prospectively compared patients with rectal cancer undergoing neoadjuvant CRT followed by radical surgery after 6 or 12 weeks from CRT. Although this study was not randomized and the 12-week group had significantly more advanced disease at baseline (as determined by primary tumor extension), there was a higher rate of pCR rate in this latter even though without statistical significance. Interestingly, the authors showed no increase in postoperative surgical complications among the longer interval group (12 weeks) [39].

The fear of potential metastatic dissemination when tumor is left in place for prolonged periods was used as an argument in favor of an early surgery (<8 weeks) after CRT completion. Noteworthy, tumor cell death seems to be related to a process induced by ionizing radiation. It is thought that after exposure to a dose of 44 Gy, metastatic potential of these tumors might decrease significantly because of the potential decrease in the overall number of surviving cells [40]. In recent studies it was found that prolonged intervals (>8 weeks) from CRT to surgery may not have any associated negative oncologic impact. In addition, these patients undergoing delayed surgery were actually associated with less postoperative morbidity, further supporting the safety of assessing tumor response at longer intervals [41, 42].

Tumor features and biology

Several aspects of the primary rectal cancer such as tumor height, extension and initial disease staging, have been considered to be predictors of tumor response or complete pathological response to neoadjuvant treatment. Even though very few studies have included patients with cT2N0 rectal cancer treated by neoadjuvant CRT, so far there has been no data to support that these tumors would develop pCR more frequently. Still, as experience increases with these earlier tumors being treated with CRT, there is still a chance that baseline stage is indeed a predictor of response to CRT.

In one retrospective study of over 500 patients tumor extension was an independent predictive factor of pCR after neoadjuvant CRT. In this study, circumferential tumor extent of $<60\%$ was significant predictor of pCR. Even though tumor distance from the anal verge was not a predictor of pCR, tumors located in the distal 5 cm of the rectum were more likely to develop greater tumor downstaging [43].

There is a hope that molecular biology will have a significant role in providing additional information and perhaps predicting tumor response to neoadjuvant CRT. Until now, only a few studies have addressed the role of gene expression in predicting response to CRT [44–46]. These studies generally compared "good" to "bad" responders. The problem is that while some of them considered only patients with pCR (as "good" responders), others grouped together patients with significantly different ypTNM stage classification

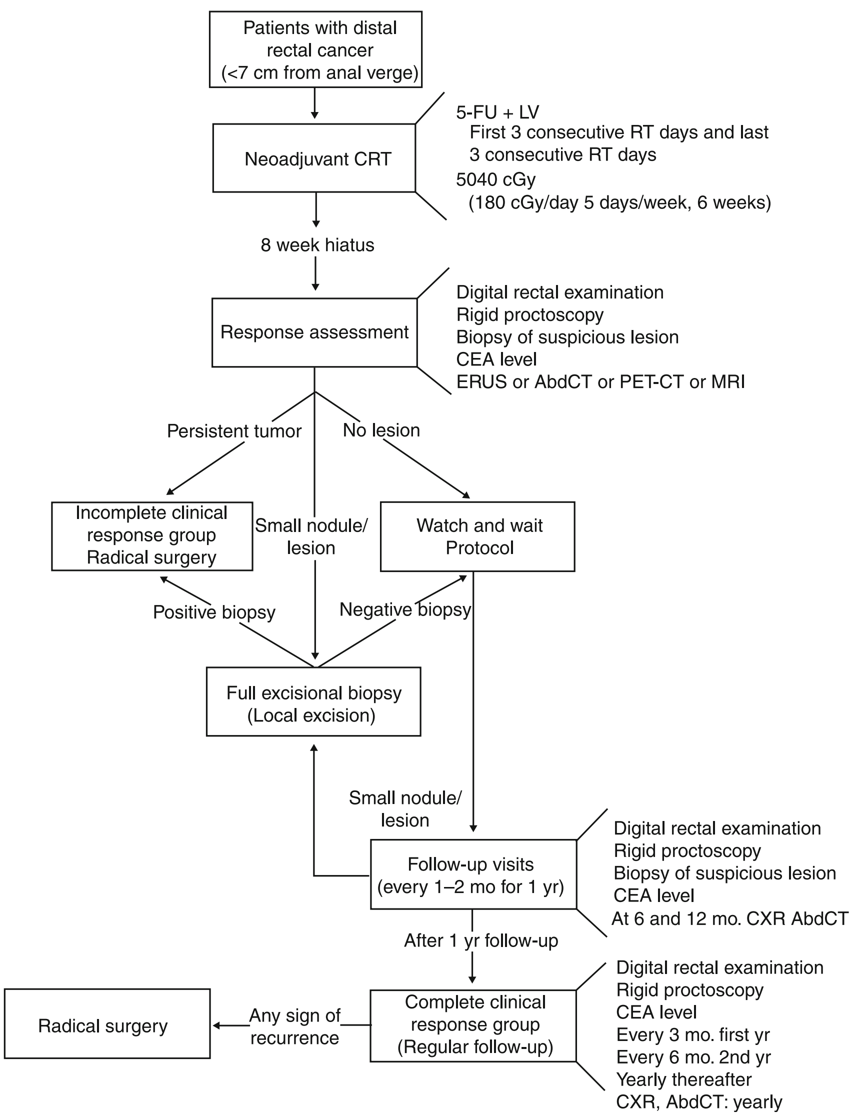

Fig. 4. The Watch & Wait Algorithm

as long as less than 10% of tumor cells were present ("good" response was based on tumor regression grading systems). The end-result is that all three studies suggested a set of genes capable of predicting a "good response" without a single gene in common between them [47]. More recently, it has been observed an strong association with some genes mutation (k-ras, p53 and others) and the absence of pCR [48]. Further studies using more advanced technologies in gene expression analysis are warranted in order to provide more definitive and useful information.

The Watch & Wait Protocol

Patients with complete clinical response, either after clinical assessment or after transanal local excision with complete primary tumor regression (ypT0), are enrolled in a strict follow-up program with no immediate surgery (Fig. 4). Adherence to the program is critical because distinguishing between complete and near-complete responses may sometimes be difficult and final decision might only be possible after a few follow-up visits. This is why an empirical 12-month probation period has been suggested where only patients that sustain a complete clinical response are considered as true cCR's [49].

The algorithm includes monthly follow-up visits with digital rectal examination and rigid proctoscopy in every visit for the first 3 months and every two to three months during the rest of the first year. CEA levels are determined every 2 months. Other radiological studies, including pelvic CT scans or magnetic resonance imaging, are performed at the time of initial tumor response assessment, and then every 6 months if there are no signs of tumor recurrence. Again, the main objective of these radiological studies is to rule out any sign of residual extrarectal disease, such as residual nodal disease that would require further investigation or even radical resection. The use of PET CT has not yet been standardized in the protocol, even though the metabolic information provided by it is useful in some cases.

Patients are fully informed that complete clinical regression of their primary tumor may be temporary and disease recurrence or tumor regrowth may occur at any time during follow-up. In the case of obvious recurrence or tumor regrowth, radical surgery is strongly recommended. Small nodules or scars may develop over time and can be managed by full-thickness transanal excision (either standard or Transanal Endoscopic Microsurgery), primarily as a diagnostic approach.

After 1 year of sustained, complete clinical response, patients are recommended for follow-up visits every 3 months, using the same clinical assessment tools used at initial patient assessment.

This treatment strategy has evolved since the beginning of our experience in 1991. Our accuracy in clinical assessment of tumor response has probably improved significantly with growing experience. At the beginning of our experience, patients were more frequently followed without immediate surgery when a near-complete clinical response was considered expecting that time would lead to a complete clinical response. More recently, these patients have been better assessed using full-thickness local excision (FTLE) as a diagnostic procedure, and according to the pathologic report they are then either managed by strict observation or referred to immediate radical surgery. Availability of surgical techniques such as TEM has also lowered the trigger for FTLE in the presence of questionable residual lesions.

Results

Many patients in our series have still been operated on and found to have ypT0N0 (absence of residual tumor) after radical surgery. It is possible, that incorporation of TEM (Transanal Endoscopic Microsurgery) for diagnostic or assessment of tumor response purposes would lead to a significant decrease in the rates of pCR following radical operations. Still, this is yet to be demonstrated.

In order to understand if there was any oncological benefit of radical surgery in the setting of complete tumor regression, a retrospective study was carried out at our Institution where patients with complete pathological response (pCR) managed by radical surgery were compared to patients with cCR managed non-operatively [50].

Patients managed by observation alone had similar outcomes to those managed by radical surgery in terms of long-term survival. Local recurrences were higher in the observation group. However, all recurrences were confined to the rectal wall and amenable to surgical salvage. No exclusive pelvic relapses without endorectal component was observed.

Five-year overall and disease-free survival rates were associated to disease final stage (clinical or pathological) and were 88% and 83% in pCR group and 100% and 92% in cCR group. These excellent survival rates in patients stage pCR and cCR were significantly better than those observed in patients ypII and ypIII. Patients with stage ypI had intermediate results.

An interesting observation is that in our series, systemic recurrences in cCR patients occurred considerably earlier than local recurrences. Besides intrinsic tumor behavior, this could be partly explained by the staging inaccuracy of the different available imaging modalities, which were probably not capable of detecting microscopic foci or metastatic disease at initial presentation.

Also, local recurrences were observed in 10% of patients managed nonoperatively after a cCR and developed considerably later during follow-up. This has also been observed in other series, where more than one third of patients who develop local recurrences after neoadjuvant CRT and radical surgery, did so after 5 years of follow-up. In contrast, 75% of patients that develop local recurrences after radical surgery alone, do so within 2 years of follow-up. This information may have implications when considering follow-up and surveillance strategies [51].

Up to now, all local recurrences in patients with cCR after neoadjuvant CRT were amenable to salvage therapy. These recurrences and their salvage procedures were performed at considerably long intervals after CRT completion (mean > 50 months). In almost half of the cases an abdominoperineal resection (APR) was performed. Also, a third of these patients presented with low and superficial recurrences, amenable to full thickness transanal excision [51].

A significant subgroup of patients, presented early tumor regrowth (within 12 months from CRT completion). These patients were most commonly misdiagnosed as cCR and had their definitive surgical treatment postponed for variable periods of time. This raised the question whether these patients could have been harmed from an oncologic standpoint by delaying definitive surgical resection. However, long-term data revealed that they fared no worse than patients with incomplete clinical response and managed by radical surgery after 8 weeks from CRT completion. Noteworthy, final pathology in this group revealed significant tumor downstaging and even lower rates of lymph node metastases, further supporting the idea that downstaging is a time-dependent phenomenon. The fact that these patients were more frequently managed by APR, could reflect a motivation (both by the surgeon and the patient) to delay final decision on radical resection, knowing that tumor regression could be still going on [42].

Evolution: The extended chemoradiotherapy regimen

In order to increase the rates of tumor response, the delivery of chemotherapy during the waiting or resting period between radiation completion and tumor response assessment has been implemented in our Institution. This regimen consists of 45 Gy of radiation delivered by a three-field approach with daily doses of 1.8 Gy on weekdays to the pelvis, followed by a 9-Gy boost to the primary tumor and perirectal tissue (54 Gy total). Concomitantly, patients receive three cycles of bolus 5FU (450 mg/m^2) and a fixed dose of 50 mg of leucovorin for three consecutive days every three weeks. After completion of radiation, patients receive three additional identical cycles of chemotherapy every three weeks (21 days) during nine weeks. Tumor response assessment is performed immediately at 10 weeks from radiation completion (Fig. 5).

In a preliminary report of our series including T2/T3 distal rectal cancers, the sustained complete clinical response rate (>12 months) was 65% with no significant increase in chemotherapy-related toxicity rates [52].

Perspectives

Many are the aspects in the management of complete clinical response after neoadjuvant CRT that remain unresolved and that should be focus of future research.

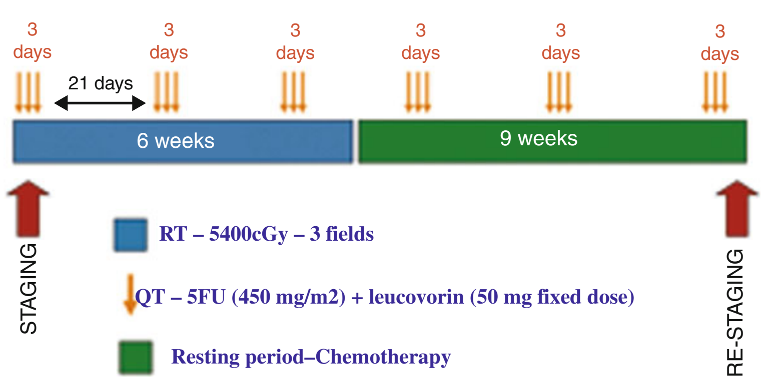

Fig. 5. The Extended Chemoradiation Regimen

Ongoing prospective randomized trials comparing different intervals between CRT completion and tumor assessment may provide additional information regarding this particular issue in rectal cancer management. Also, perhaps data from PET/CT imaging at different intervals from CRT completion may indicate kinetics of tumor metabolism as function of time in these patients.

Novel radiation therapy regimens including alternative radiation doses, delivery methods, and technical variants to maximize radiation-related tumor cell death and minimize side effects is an area of special interest. Moreover, improved chemotherapy regimens might lead to an increase in the rate of complete clinical response and, maybe, improve survival rates. Some investigators have suggested the use of aggressive induction chemotherapy before the delivery of radiation to provide immediate treatment of undetected microscopic foci of metastatic tumor cells in addition to the primary tumor. These regimens are currently under investigation in controlled trials to provide data on safety and long-term benefits [53].

Finally, development of next generation gene sequencing technology may allow further understanding of molecular genetic events relevant to sensitivity or resistance to neoadjuvant CRT. Identification of gene signatures may allow improvement of patient selection leading to true individualized management decisions. There is hope that studies using RNAseq technology may provide more definitive information in the near future.

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Surgery of low rectal cancer: Intersphincteric resection and its modifications

Surgical anatomy in intersphincteric resection

Yusuke Kinugasa and Yoshihiro Moriya

Introduction

Recently, surgical techniques for low rectal cancer have greatly progressed, thereby increasing the rate of sphincter preservation. As a result of the development and spread of surgical procedures including the total mesorectal excision (TME) [1] and intersphincteric resection (ISR) [2], rectal surgeons more frequent have the opportunity to observe the anorectal junction and to mobilize the distal rectum to the anal canal. Knowledge about the anatomical structures in the lower pelvis is important for the abdominal and perineal parts of ISR.

However, critically controversial descriptions of the fascial structures in the pelvis are common, except for the concept that the mesorectum is surrounded by visceral fascia or the fascia propria of the rectum [3]. Controversies exist with regard to which fascia covers the hypogastric nerve (HGN) and whether the rectosacral fascia is a real structure or a surgical artifact due to adhesion of the fasciae. Moreover, it is unclear whether the presacral fascia and Waldeyer's fascia are the same fascia [4]. As Range and Woodburne [5] pointed out the possibility that pelvic fascial structures are easily developed during dissection and surgery, a comprehensive histological study using large sections covering wide areas around the mesorectum seems necessary. We performed histological studies to try and resolve the aforementioned controversies.

It is important to thoroughly understand the morphology of the connective tissue structures around anal canal in order perform ISR and many other procedures. The rectourethralis muscles and the anococcygeal ligament are important structures at the anorectal junction for ISR. These structures are located between surgical planes by both the abdominal and peranal approach. The following descriptions will be useful for surgeons performing ISR and other procedures that affect the same region.

Fascial structures around the rectum (Figs. 1, 2)

To avoid presacral venous bleeding, autonomic nerve injury and local recurrence, mobilization of the rectum is performed by anatomical dissection along the fascial planes [6, 7]. Therefore, a comprehensive understanding of the fascial structures around the rectum is critically important for rectal surgeons.

Fascia propria of the rectum

The fascia propria of the rectum is a thin visceral fascia covering the rectum and mesorectum. The mesorectum is a distinct compartment that contains the superior rectal arteries and veins, mesorectal fat, lymphatic vessels and nodes. This fascia is also called the perirectal fascia, rectal fascia, and visceral fascia.

Denonvilliers' fascia (Fig. 3)

Denonvilliers' fascia is clearly identifiable in males between the fascia propria of the rectum and the seminal vesicles or prostate. The rectovaginal septum in females corresponds to Denonvilliers' fascia. The consistency of Denonvilliers' fascia varies between individuals, from a fragile translucent layer to a tough leathery membrane [8]. The rectovaginal septum is less prominent in females than Denonvilliers' fascia is in males. The fascia is thicker in younger individuals and then thins out with age, and it may be more obvious in patients with preoperative radiotherapy to the pelvis or with transmural inflammation of the rectum (i.e. Crohn's disease) [9].

Laterally, Denonvilliers' fascia divides into several thin laminae, and one of the lateral continuations extends

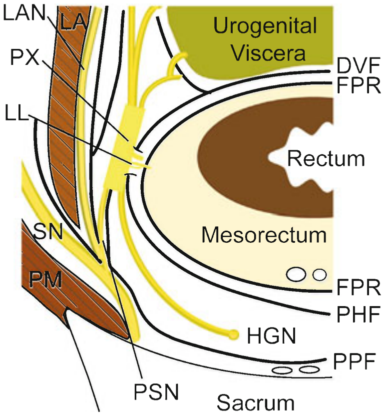

Fig. 1. Schematic representation of fasciae around the rectum (horizontal)

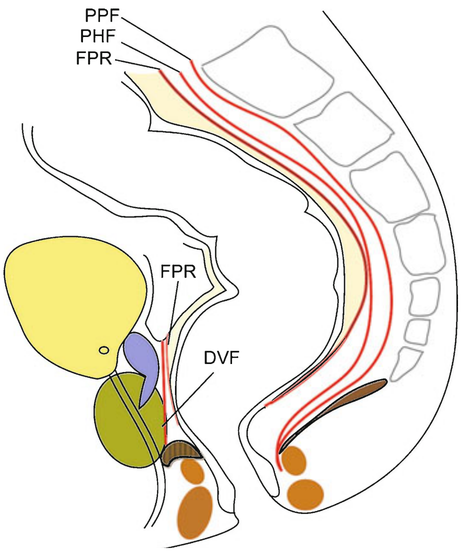

Fig. 2. Schematic representation of fasciae around the rectum (sagittal). *DVF* Denonvilliers' fascia; *FPR* fascia propria of rectum; *HGN* hypogastric nerves; *LA* levator ani muscle; *LAN* levator ani nerve; *LL* lateral ligament; *MR* mesorectum; *PHF* pre-hypogastric nerve fascia; *PM* piriformis muscle; *PPF* parietal presacral fascia; *PSN* pelvic splanchnic nerves; *PX* pelvic plexus; *SN* sacral nerve

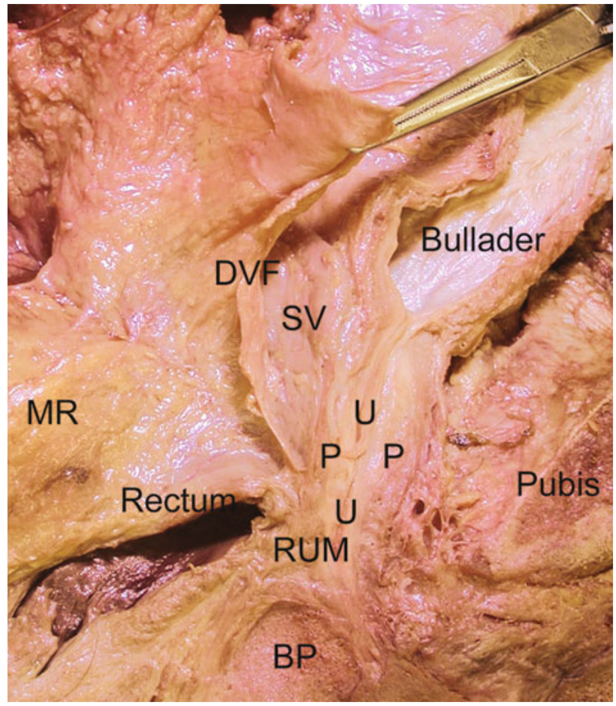

Fig. 3. Sagittal section of the male left hemipelvis. Panel displays anterior mobilization of the rectum, with separation of the Denonvilliers' fascia (DVF) from the mesorectum and prostate (P). *MR* Mesorectum; *RUM* rectourethralis muscle; *SV* seminal vesicle; *U* urethra

dorsolaterally and separates the mesorectum from the pelvic plexus and urogenital neurovascular bundle [10]. The caudal part of the Denonvilliers' fascia joins the prostate or rectourethral muscle, and for that reason, it is more easily separated from the rectum than from the prostate.

Pre-hypogastric nerve fascia

The pre-hypogastric nerve fascia is variously known as the urogenital fascia [11], hypogastric nerve sheath, or ureterohypogastric fascia [12]. This fascia is located immediately behind the fascia propria of the rectum, covering the right and left hypogastric nerves [3] and also the pelvic plexus, and connecting with the lateral continuations of Denonvilliers' fascia at the level of the pelvic plexus (Fig. 1). The left ureter runs dorsal to the pre-hypogastric fascia, while the right ureter runs ventral to the fascia [13].

Parietal presacral fascia

The parietal layer of the presacral fascia (synonym, Waldeyer's fascia [9]) is located dorsal to the hypogastric nerves and ventral to the sacral veins and iliac vessels, and divides into several parietal pelvic fasciae extending ventro-laterally, including: (1) the fasciae lining or enclosing the pelvic plexus; (2) the fasciae providing a posterior attachment for the levator ani muscle and lining the medial or superior surface of the muscle sheet; and (3) the fasciae enclosing the pudendal nerve and associated inferior gluteal and internal pudendal vessels [3]. The most medial fascia covers the pelvic splanchnic nerves and fuses with the pre-hypogastric nerve fascia at the pelvic plexus.

Rectosacral fascia

The rectosacral fascia is not a true fascial structure, but it represents part of any thickened pelvic fascia [9] or adhesion of connections between the layers of fasciae existing posterior to the rectum, including the fascia propria of the rectum, the pre-hypogastric nerve fascia [3], or the parietal pelvic fascia [14]. Clinically, however, a band is apparent between the posterior wall of the rectum and the sacrum at 3–5 cm above the anorectal junction, or higher, as described by Havenga et al. [15]. This fascia should not be confused with Waldeyer's fascia, which only refers to the most distal portion of the presacral fasciae joining the anorectal junction [4].

Autonomic nerves (Fig. 4)

Sympathetic supply to the rectum and upper anal canal originates in the first and second lumbar spinal segments. The fibers are distributed through the inferior mesenteric plexuses via the lumbar splanchnic nerves, and through the pelvic plexus via the sacral splanchnic nerves. Parasympathetic nerves are supplied to the rectum through the pelvic plexus via the pelvic splanchnic nerves [16].

The pelvic urogenital autonomic nervous system is present immediately outside the rectum. Nerve-sparing surgery aims to preserve several major nerve structures in the pelvis, including peripheral nerve bundles such as the hypogastric nerves, pelvic splanchnic nerves and cavernous nerves.

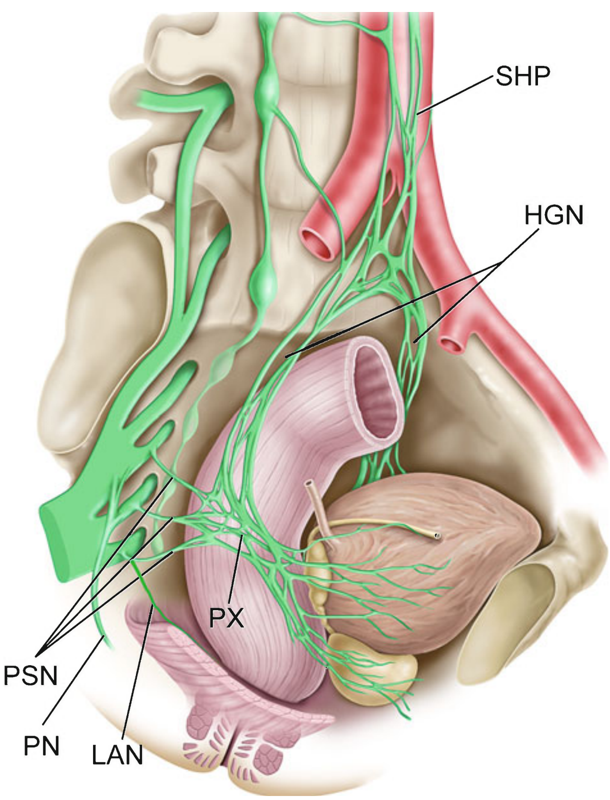

Fig. 4. Topographic anatomy of the pelvic autonomic nerves. *HGN* hypogastric nerves; *LAN* levator ani nerve; *PN* pudendal nerve; *PSN* pelvic splanchnic nerves; *PX* pelvic plexus; *SHP* superior hypogastric plexus

Superior hypogastric plexus

The superior hypogastric plexus is a network of sympathetic pre- and post-ganglionic fibers emerging from the second to fourth lumbar splanchnic nerves and located 3–7 cm caudal to the origin of the inferior mesenteric artery and just caudal to the bifurcation of the aorta [17]. The plexus extends down about 4 cm with fine nerve fibers to the rectum and divides into the right and left hypogastric nerves.

Hypogastric nerves

The hypogastric nerves represent extensions of the sympathetic nerves dividing from the superior hypogastric plexus, and then extending down along the pelvic wall under the pre-hypogastric nerve fascia to connect the pelvic plexuses, while sending small rectal branches around the superior rectal artery penetrating through two fasciae: the pre-hypogastric nerve fascia, and the fascia propria of the rectum. The hypogastric nerves play a role in ejaculatory function, causing closure of the internal ostium of the urethra and constriction of the internal sphincter muscles. According to the severity of damage to the hypogastric nerves, various disturbances of ejaculatory function may develop, including retrograde ejaculation.

Pelvic splanchnic nerves

The pelvic splanchnic nerves, which are parasympathetic nerves, form as branches of the second, third, and fourth (mainly the third and fourth) sacral nerves emerging from the anterior sacral foraminae on either side. The pelvic splanchnic nerves, which often form a common trunk with the levator ani nerves at their origin, run to the target pelvic organs via the pelvic plexus and to the sigmoid and descending colon as far as the splenic flexure and distal transverse colon, along to the inferior mesenteric artery and left colic artery. These nerves activate the smooth muscle of the rectum, anus and bladder wall and inhibit the vesical sphincter.

The cavernous nerves (nervi erigentes) supply vasodilator fibers to the erectile tissue of the penis and clitoris, and arise mainly from the fourth pelvic splanchnic nerve, and run in the neurovascular bundles posterolateral to the prostate [18] where they penetrate the rectourethralis muscle posterior to the anorectal junction in about half of cases [19].

Pelvic plexus

The pelvic plexus, also known as the inferior hypogastric plexus, appears as a mesh-like triangle located under the pre-hypogastric nerve fascia on the pelvic side walls anterolateral to the rectum and posterolateral to the seminal vesicles, prostate and urinary bladder in males, and lateral to the uterine cervix, vaginal fornix and bladder, and often extending into the broad ligaments of the uterus in females. This plexus is mainly formed by the hypogastric nerves and pelvic splanchnic nerves, and sends nerve branches arising at the anteroinferior corner of the plexus to the genitourinary organs, running with the blood vessels (neurovascular bundles).

Levator ani nerves

The levator ani nerves represent one of the components of the pudendal plexus. The origins of the nerves often form a common trunk with the pelvic splanchnic nerves, and extend down along the levator ani under the thick parietal pelvic fascia (levator ani fascia), sending branches to the muscles. Injury to the levator ani nerves means that the dissection has deviated from the recommended plane, within the distal pelvis, and therefore may result in either urinary or fecal incontinence [20].

Pudendal nerves

The pudendal nerves, which are mainly sensory nerves for the perineum, arise from the sacral plexus (second to fourth sacral nerves) leave the pelvic cavity through the greater sciatic foramen, enter the gluteal region, cross the sacrospinous ligament close to the ischial spine and run through the pudendal canal (Alcock's canal) toward the ischioanal fossa. These nerves then divide into the inferior rectal, perineal, and dorsal nerves of the penis or clitoris.

Muscles and structures around the anal canal

Anal canal

The anal canal begins at the anorectal junction and ends at the anal verge. It is angulated in relation to the rectum because the pull of the sling-like puborectalis produces the anorectal angle. It lies 2–3 cm in front of, and slightly below, the tip of the coccyx. The pigmentation of the skin around the anal verge approximately corresponds to the extent of the external anal sphincter. Identification of the anal verge may sometimes be difficult. The functional anal canal is represented by a zone of high pressure which roughly equates to the anatomical canal. The anal canal consists of an inner epithelial lining, a vascular subepithelium, the internal and external anal sphincters and fibromuscular supporting tissue, as well as dense neuronal networks of both autonomic and somatic origin. It ranges from 2.5 and 5 cm in length in adults, although the anterior wall is slightly shorter than the posterior. It is usually shorter in females.

The upper portion of the anal canal is lined by columnar epithelium similar to those of the rectum. It contains secretory and absorptive cells with numerous tubular glands or crypts. Terminal branches of the superior rectal vessels pass downwards towards the anal columns. The submucosal veins drain into the submucosal rectal venous plexus and also through the fibers of the upper internal anal sphincter into an intermuscular venous plexus. Each column contains a terminal radicle of the superior rectal artery and vein. The vessels are largest in the left-lateral, right-posterior and right-anterior quadrants of the wall of the canal where the subepithelial tissues expand into three ‘anal cushions’. The cushions help to seal the anal canal, to maintain continence to flatus and fluid, and are also important in the pathogenesis of hemorrhoids. The anal valves and sinuses together form the dentate (or pectinate) line at the lower ends of the columns [7].

Levator ani muscle

The levator ani muscle is a muscular sheet which is attached to the internal surface of the pelvis and it forms a large portion of the pelvic floor. The muscle is subdivided into named portions according to their attachments and the pelvic viscera to which they are related. The separate parts are referred to as the iliococcygeus, pubococcygeus and puborectalis. These parts are often referred to as separate muscles, but the boundaries between each part cannot be easily distinguished, and they perform many similar physiological functions. The levator ani arises from each side of the walls of the pelvis along the condensation of the obturator fascia (the tendinous arch of the levator ani). Closer to the anorectal junction and elsewhere in the pelvic floor, the fibers are more nearly continuous with those of the opposite side, and the muscle forms a sling (puborectalis).

Rectourethralis muscle (Fig. 5)

In males, the rectourethralis muscle, which is a mass of smooth muscle, occupies a space encircled by the urethra, rhabdosphincter (external urethral sphincter), external rectal muscularis propria and bilateral levator ani slings [21]. The external anal sphincter is likely to be tightly connected to the rectourethralis muscle, and the rectal muscularis propria communicates with the rectourethralis muscle [19]. The rectourethralis muscle provides posterior attachment for the rhabdosphincter. Denonvilliers' fascia ends at the rectourethralis muscle. The anorectal veins take a tortuous course across the rectourethralis muscle. Moreover, the cavernous nerve has been reported to penetrate the rectourethralis muscle [22]. Therefore, careful treatment of this muscle seems to be necessary to avoid inducing male sexual dysfunction.

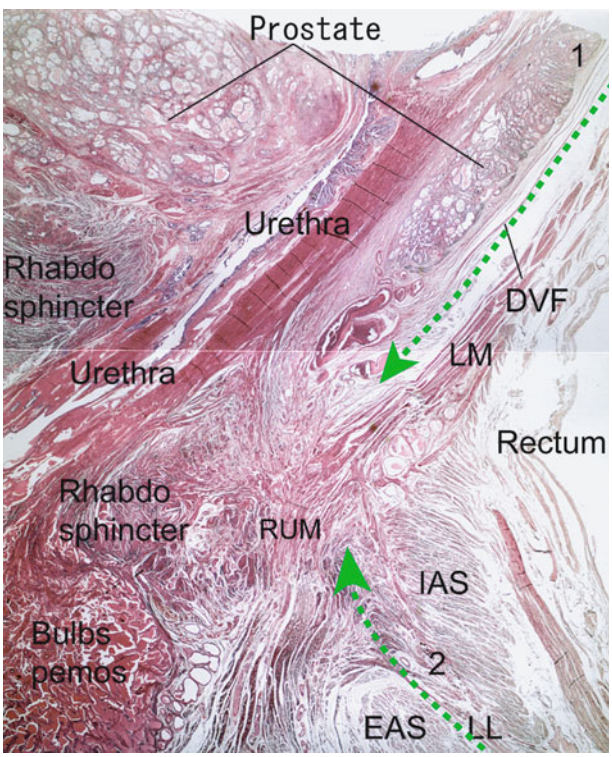

Fig. 5. Histological observation of the rectourethralis muscle (Sagittal section). Surgical planes are shown as dotted lines. (1) Surgical plane by abdominal approach; (2) Intersphincteric resection (by peranal approach); *DVF* Denonvilliers' fascia; *EAS* external anal sphincter; *LL* Longitudinal layer; *IAS* internal anal sphincter; *RUM* rectourethralis muscle

Anococcygeal ligament (Fig. 6)

The anococcygeal ligament extends from the coccyx to the anal canal between bilateral slings of the levator ani [23]. The anococcygeal ligament is divided into a ventral and a dorsal layer and contains abundant smooth muscles, elastic fibers, and small vessels. The ventral layer extends from the presacral fascia to the conjoint longitudinal layer of the anal canal. The dorsal layer is recognized as a bundle extending between the coccyx and external anal sphincter. The dorsal layer is much thicker along and near the midsagittal area than the lateral areas.

ISR for the lower rectal cancer requires division of the fibers (ventral layer) of the anococcygeal ligament extending into the internal anal sphincter. A sharp resection of the anococcygeal ligament from an abdominal view may sometimes be difficult for tumors occupying the posterior wall of the rectum. However, choosing a dorsal plane distant from the ligament may cause an injury to the external anal sphincter. The peranal approach along the ventral aspect of the external anal sphincter may mislead a surgeon to an artificial space between the ventral and dorsal layers of the anococcygeal ligament. This plane is deeper than the abdominal approach in many cases.

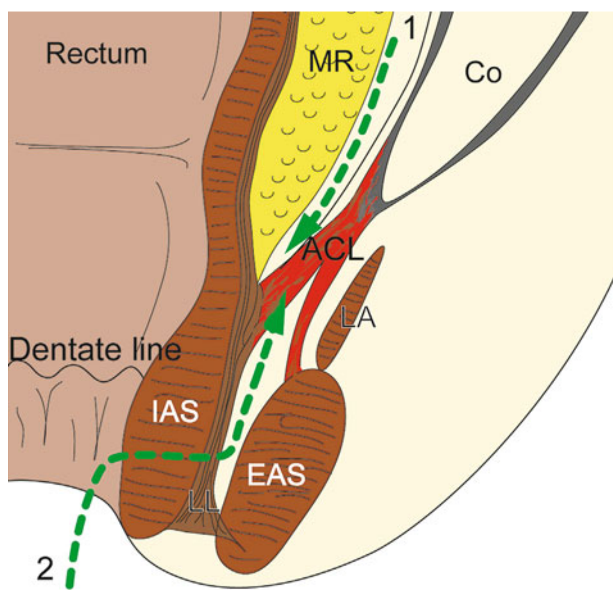

Fig. 6. Schematic representation of the anococcygeal ligament. Surgical planes are shown as dotted lines. (1) Surgical plane by abdominal approach; (2) Intersphincteric resection (by peranal approach); *ACL* anococcygeal ligament; *Co* coccyx; *EAS* external anal sphincter; *IAS* internal anal sphincter; *LA* levator ani; *LL* conjoint longitudinal muscle layer of the anal canal; *MR* mesorectum

Recognition that a rough separation of the anococcygeal ligament and rectal wall may cause injury or even a perforation of the rectal wall is therefore important.

Internal anal sphincter

The internal anal sphincter consists of orientated smooth muscle fibers that are continuous with the circular muscle of the rectum, and which terminate at the junction of the superficial and subcutaneous components of the external sphincter. Its thickness varies between 1.5 and 3.5 mm, depending upon the height within the anal canal and whether the canal is distended. It is usually thinner in females and becomes thicker with age. It may also be thickened in disease processes such as rectal prolapse and chronic constipation. The lower portion of the sphincter is crossed by fibers from the conjoint longitudinal muscles, which pass into the submucosa of the lower canal. The internal anal sphincter is supplied by the sympathetic and parasympathetic systems by fibers that extend down from the lower rectum. Sympathetic fibers originate in the lower two lumbar spinal segments, they are distributed via the pelvic plexus, and thus cause contraction of the sphincter. The parasympathetic fibers originate in the second to fourth sacral spinal segments, are distributed via the pelvic plexus, and cause the relaxation of the sphincter [7].

External anal sphincter

The external anal sphincter is a complex of striated muscle composed mainly of type 1 skeletal muscle fibers, which are well suited to prolonged contraction. It has been described as consisting of deep, superficial and subcutaneous parts. The uppermost fibers blend with the lowest fibers of the puborectalis. In the upper third, some of these upper fibers decussate anteriorly into the superficial transverse perineal muscles, and posteriorly, some fibers are attached to the dorsal layer of the anococcygeal ligament. The majority of the fibers of the middle third of the external anal sphincter surround the lower part of the internal anal sphincter [2, 24]. The middle third is attached anteriorly to the rectourethralis muscle and posteriorly to the coccyx via the anococcygeal ligament. The length and thickness of the external anal sphincter varies between the sexes. In females, the anterior portion tends to be shorter, and the wall may be slightly thinner. The external anal sphincter is innervated mainly by the inferior rectal branch of the pudendal nerve. It may also receive some direct supply via fibers which leave the ventral branch of these nerves as they exit the sacral foramina and run beneath the fascia over the levator ani to reach the anorectal junction.

Conjoint longitudinal muscle layer of the anal canal

The longitudinal layer is situated between the internal and external sphincters [7]. It contains a fibromuscular layer, the conjoint longitudinal coat, and the intersphincteric space with its connective tissue components. The longitudinal layer has muscular and fibroelastic components. The muscular element is formed by fusion of striated muscle fibers from the puborectalis, with smooth muscle from the longitudinal muscle of the rectum. In males, these often end just above the lower border of the internal anal sphincter. The layer then becomes completely fibroelastic, and splits into septa running between bundles of the subcutaneous external anal sphincter to terminate in the perianal skin. The most peripheral of the septa extend between the fibers of the external sphincter into the ischio-anal fat. The most central septa pass through the fibers of the internal anal sphincter to reach the anal lining, and may help to form the intersphincteric groove. The conjoint longitudinal coat is innervated by autonomic fibers that share an origin with the fibers that innervate the internal anal sphincter.

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The history of rectal resection: The quest for sphincter preservation

Brigitte Kovanyi-Holzer

Introduction

Intersphincteric resection is an extreme type of sphincter salvage for low rectal tumors.

The technique combines total mesorectal excision with transanal intersphincteric resection of the internal sphincter and the lower rectum. Continuity of the bowel is restored by performing a coloanal anastomosis.

Perineal approach

The quest for sphincter-saving surgery in patients with tumors of the lower rectum has a long history and has led to a number of diverse surgical approaches.

The first operations for carcinoma of the rectum were performed by the transperineal approach and are attributed to Faget (1739), Lisfranc (1826) (Fig. 1), and Verneuil (1837) [1–3]. The outcome of these operations – which were performed by the extraperitoneal approach – was fatal in most patients because they developed sepsis.

In 1907 Lockhart-Mummery evolved the method into a useful mode of cancer surgery, which is also known as perineal excision [4]. By this method it was possible to remove about 22–25 cm of the rectum and the distal sigmoid. The principal features of this procedure were its safety and simplicity.

A two-stage operation was performed: after creating of a two-fold colostomy in the left iliac fossa, during which the peritoneal cavity was inspected for metastases and the operability of the tumor was established, a perineal resection was performed two or three weeks later after the portion of the bowel to be resected had been irrigated via the colostomy. The distal end of the portion of the bowel proceeding from the final colostomy was closed. This mode of treating rectal carcinoma has two disadvantages: stool tends to accumulate in the portion of the bowel with a blind end, located distal to the colostomy, and it is difficult to remove tumors located above the proximal third of the rectum. Nevertheless, perineal resection of the rectum became an established method and remained the surgical procedure of choice in the USA and Great Britain until the thirties of the twentieth century. During this time – in the era prior to blood transfusion and antibiotics – a study performed in 1932 showed that the method achieved an operability rate of 50%, was associated with a mortality rate of 12% and a five-year survival rate of 40% [5].

Sacral approach

Sacral excision was most popular in Germany and Austria. It was an extension of perineal excision by removal of the coccyx and the lowermost part of the sacrum. The approach provided good access to the posterior aspect of the rectum above the levator muscles and also permitted restoration of bowel continuity. Kocher described transsacral excision in 1874. By performing an oblique incision from the anus to the coccyx, followed by removal of the coccyx, the peritoneum could be opened, the bowel pulled downward, the rectum and the anal canal removed as a whole, the distal colon shifted to the sacral region, and an artificial sacral anus could be placed [6]. Kraske modified trans-sacral excision in that he tried to anastomose the sigma with the preserved stump of the rectum, but the anastomosis was nearly always insufficient [7]. A drawback of this method was the end-to-end anastomosis by a simple circular suture, which was very prone to rupture and the formation of fecal fistulas. To avoid this complication Hochenegg (Fig. 2) developed an alternative technique in Vienna, which was published 1888. It consists of sphincter-saving resection of the rectum and was named a "pull-through ("Durchzug") procedure" [8]. Modifications of this procedure are still in use today. Hochenegg preferred to have the patient on the left side with the legs drawn upward, and used lumbar anesthesia. He always performed a parasacral incision. Depending

Fig. 1. Jacques Lisfranc: 1790–1847, French surgeon

Fig. 2. Julius von Hochenegg: 1859–1940 in Vienna

on local conditions, the following options existed for resection of the affected portion of the rectum:

1. Placement of a sacral anus with an
2. Anastomosis of the preserved stump of the rectum by means of the
3. Pull-through method

In patients who were candidates for a pull-through procedure, Hochenegg everted the anal portion and resected the mucosa. Through the excoriated anal canal the proximal colon was pulled through and sewn carefully to the anoderm. A second row of sutures was performed to join the upper end of the anal portion with the pulled-through portion of the colon. Contraindications for this technique were extensive tumors that were fixed to surrounding organs. It should be mentioned that the majority of German surgeons did not use Hochenegg's sacral method but gave preference to an abdomino-sacral access. There was, so to speak, a competition between these two surgical approaches.

In the "Wiener Klinische Wochenschrift" (translated into English: Vienna Clinical Weekly) Mandl reported on 1,704 patients with carcinoma of the rectum [9]. Of these, 984 were operated on by Hochenegg in accordance with the radical sacral procedure. A 10-year observation period revealed a mortality rate of 11%. Sixty percent of the operated patients were continent at discharge. These figures were comparable to those reported from other clinics at the time. The advantages of the method were, in addition to restoration of continence, the avoidance of suture insufficiency, fistulas, and perineal bowel prolapse.

In contrast, the "Wiener Klinische Wochenschrift" mentioned that some surgeons (including Schmieden and Kirschner) still advocated sacrificing the anal sphincter because they were, ironically, concerned about the radical nature of the operation and its functional benefits [9].

The abdominoperineal approach

Around 1908 the British surgeon William Ernest Miles reported that up to 95% of patients with carcinoma of the rectum develop recurrent disease after perineal resection [10].

Ernest Miles described a radical operation for rectal cancer that encompassed all zones of lymphatic spread of the tumor. Based on pathological studies in patients who had died of rectal cancer, he realized the need for an abdominal approach in order to control upward spread of the tumor through lymphatics running adjacent to the superior hemorrhoidal vessels. Complete resection of the tumor could be achieved by this technique. Abdominoperineal resection became the standard surgical procedure for rectal cancer and yielded a five-year survival rate of more than 50%.

The technique of perineo-abdominal excision established by Gabriel in 1934, which involved mobilization of the rectum mainly from the perineal aspect and was thus able to minimize the incision from the abdominal aspect, was unable to gain wider acceptance than Miles' technique [11].

In 1934 the German surgeon Kirschner was the first to publish a study about the feasibility of a simultaneous abdominoperineal extirpation of the rectum by two surgical teams working in parallel fashion [12]. Following subsequent developments and refinements of the procedure by Devine (1937) and Lloyd-Davies (1939), this method of surgery gained immense significance in Great Britain and the USA [13, 14].

While Miles' operation for the treatment of rectal carcinoma was established in Great Britain and the USA, the sacral access was given preference in Europe.

Miles' thesis was that, regardless of the location of a rectal carcinoma, curative treatment could only be achieved by radical abdominoperineal amputation of the rectum. Owing to this statement, the previously known sphincter-preserving methods were abandoned. After Dukes (1930), Westhues (1930, 1934), Gabriel (1934), and Gilchrist, David (1947) and Coller (1940) had presented their results it was realized that Miles' conclusions were not entirely correct; these data indicated a decisive and new pathway for sphincter-preserving rectal surgery [15–20]. Proximal tumor dissemination was observed quite frequently, whereas lateral or distal spread was extremely rare [13]. Goligher et al. (1951) (Fig. 3) observed aboral lymph node disease in just 2% of 1500 abdominoperineal resection specimens [21]. These facts led to the revival of the older sphincter-preserving surgical techniques. However, at this time it was still presumed that maintenance of continence always required a rectal stump of at least 6–8 cm. At the same time, surgeons feared intramural spread of the tumor despite the low rate of distal metastases. This necessitated a safety margin of 5 cm. Owing to these two facts, sphincter-preserving resection of the rectum was performed only in cases of tumors in the upper third of the rectum. So-called abdominosacral resection was a new technique propagated by Pannet (1935), Finsterer (1941) and Goetze (1944) in Europe [22]. Anterior resection of the rectum was developed around the same time, and was mainly refined by Dixon (1940) at the Mayo Clinic. The rectum was resected via an abdominal access and the colon was anastomosed end-to-end with the rectal stump by performing a hand-sewn suture. For a long time this procedure remained the method of choice for rectal carcinomas in high location [23].

Fig. 3. John C. Goligher

Sphincter-saving sacral resection

Sphincter-saving sacral resection was mainly used in European clinics and was associated with two disadvantages: first, leakage of the anastomosis was a common occurrence; secondly it was grossly inadequate for removal of upward lymphatic spread. The procedure of abdominosacral resection employed by Finsterer 1941 combined the advantages of APR and sphincter-saving sacral resection [22]. However, the risk of a persistent fecal fistula through the posterior wound persisted. Therefore this method failed to gained widespread acceptance.

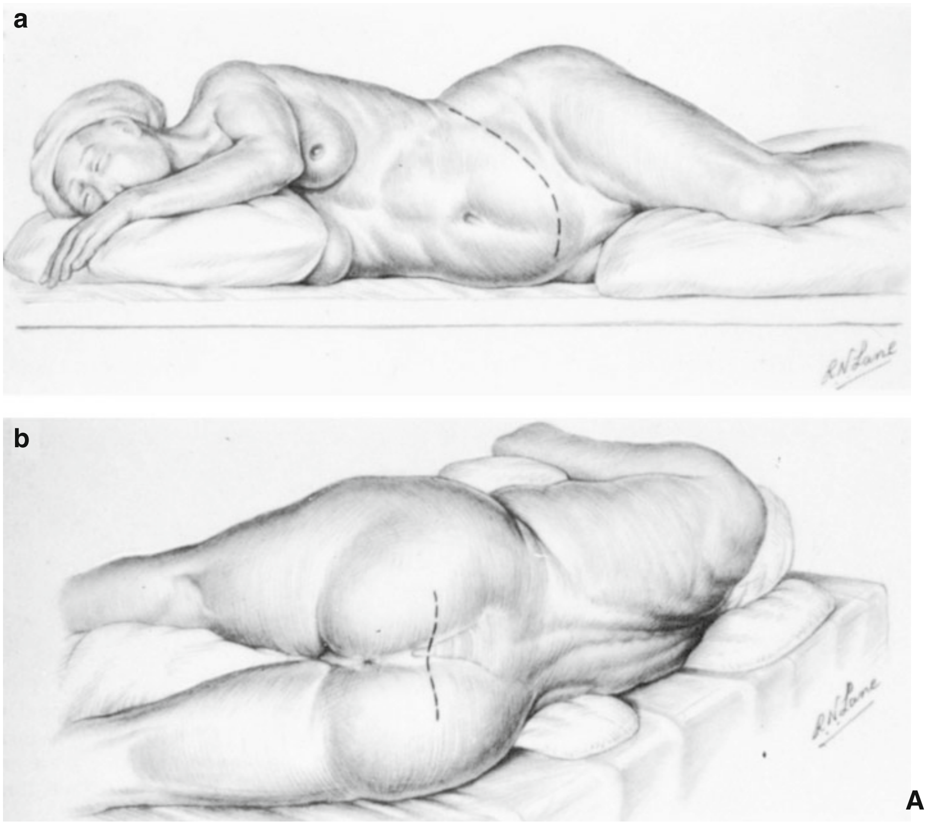
Localio and Stahl (1969) developed a special technique for performing the operation in the abdominal and the sacral phase simultaneously and synchronously. A long oblique muscle-cutting incision extending from the suprapubic region to the left loin was required for this purpose (Fig. 4) [24].

The favorable results of the so-called Mayo Clinic operation reported by Dixon in 1939 caused anterior rectum resection to become the gold standard for the treatment of tumors in the upper and middle third [23]. First attempts to resect tumors at a lower level consisted of coloanal pull-through methods, wherein the sphincter organ was primarily dissected or manually dilated so that the colon could be placed about 50 cm in front of the anus. The sphincter muscle was then sewn on the pulled-through colon and the protruding portion of the colon was resected 10 days after the operation [25].

An alternative approach consisted of eversion of the anorectal stump after resection of the cancer-bearing portion of the rectum. The colon and the anus were anastomosed externally. This procedure came to be known as the Maunsell-Weir operation. It was also propagated for a long time by Turnbull and Cutait (Fig. 5) as a means for performing sphincter-preserving resection of low rectal cancers [25, 26]. However, the drawbacks of these methods were their technical complexity and their poor results as regards the radical nature of surgery and the preservation of continence.

A trans-sphincteric approach for low rectal tumors was described by Mason [27]. He believed that division and meticulous reapproximation of the sphincter ensure adequate sphincter function. By this technique, the lower rectum is exposed and freed after previous abdominal dissection. An end-to-end anastomosis is created between the colon and the distal rectum using the convenient one-layer suture technique (Fig. 6).

The data of patients who had undergone a pull-through operation according to Babcock-Bacon or Maunsell-Weir between 1937 and 1972 were evaluated. Mortality and morbidity rates of 13% and 28%, respectively, were



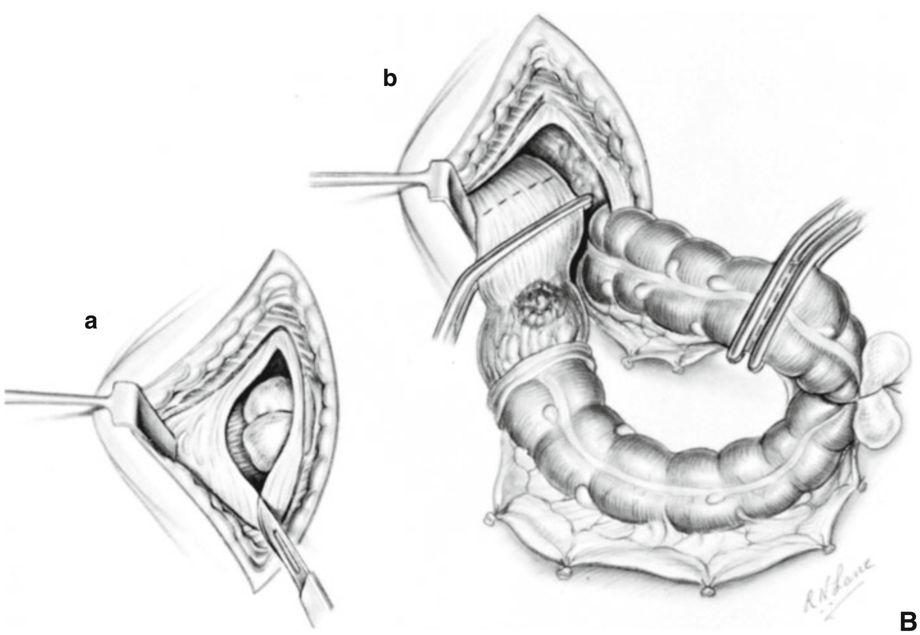


Fig. 4A. Fig. 19.109, p 685: abdominosacral resection: incision technique; **Fig. 4B.** Fig. 19.114, p 688: abdominosacral resection (**a**), sacral phase (**b**) (from John Goligher, Fifth Edition 1983, Surgery of the Anus, Rectum and Colon; Elsevier Verlag, published by Bailliere Tindall, London) established. Abscesses occurred after 41% of the operations. Insufficiency of the anastomosis was observed in 31% and local recurrences occurred after 24% of the operations. Continence could be restored in 90% of the patients [28]. In view of these rather disillusioning figures, the majority of surgeons in the nineteen-sixties and nineteen-seventies regarded abdominoperineal extirpation as the standard surgical procedure for tumors of the lower third of the rectum.

In 1972 Parks reported on an abdominotransanal operation in which the anus was dilated and the proximal colon sutured to the top of the anal canal without eversion in order to avoid damage to the anal sphincter mechanism [29]. This was a significant improvement on previous procedures. Postoperative assessment at 12–18 months revealed that nearly all patients had achieved continence to solid stool, but control of liquid stool or flatus varied [30]. This conclusion was of immense significance because it showed that the 6- to 8-cm-long rectal stump was not mandatory for preservation of continence. Thus, deeper tumors could also be treated by anterior resection.

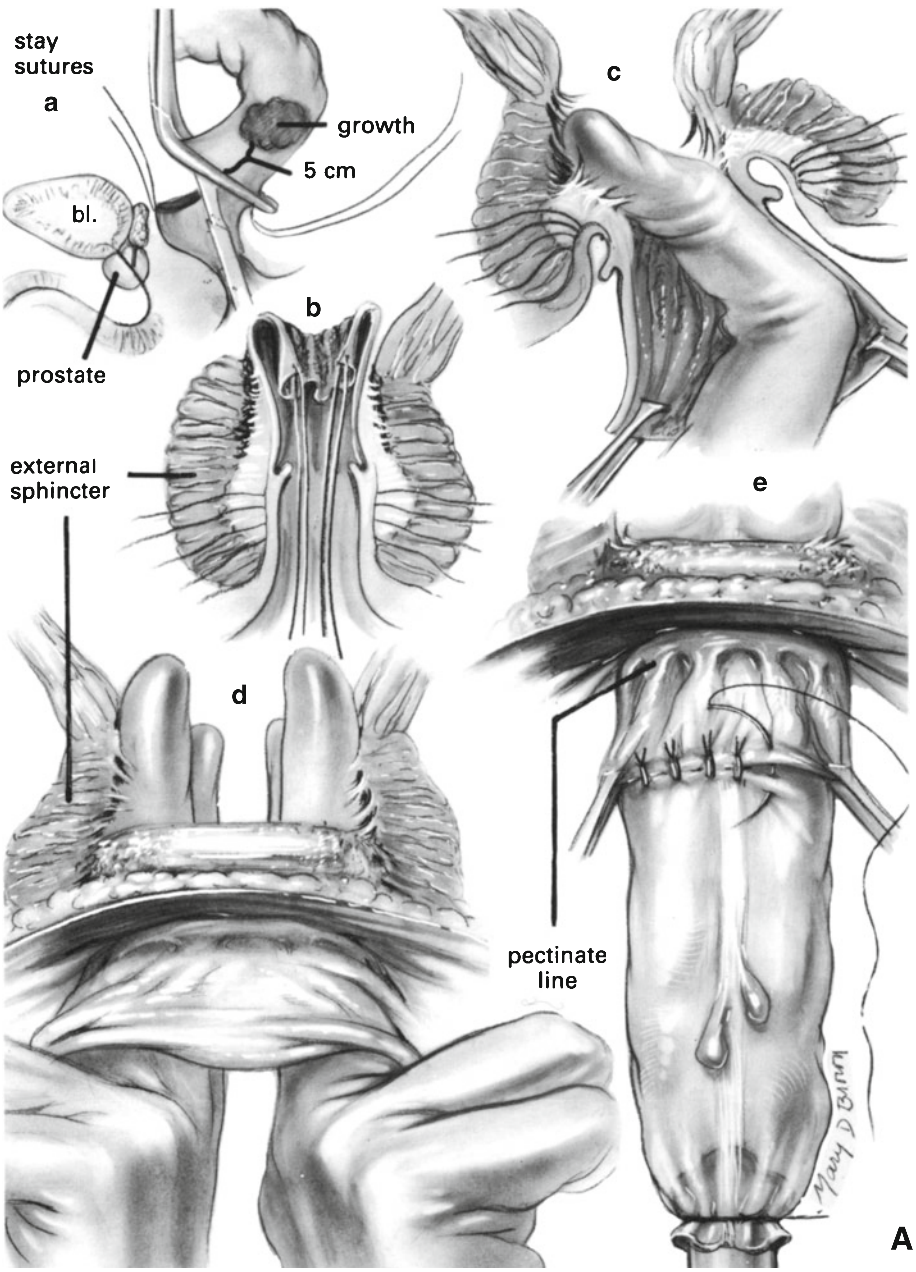


Fig. 5. Fig. 19.95 and 19.96, p 677–678: Turnbull-Cutait pull-through abdominal excision, first (**A**) and second stage (**B**) (from John Goligher, Fifth Edition 1983, Surgery of the Anus, Rectum and Colon; Elsevier Verlag, published by Bailliere Tindall, London)

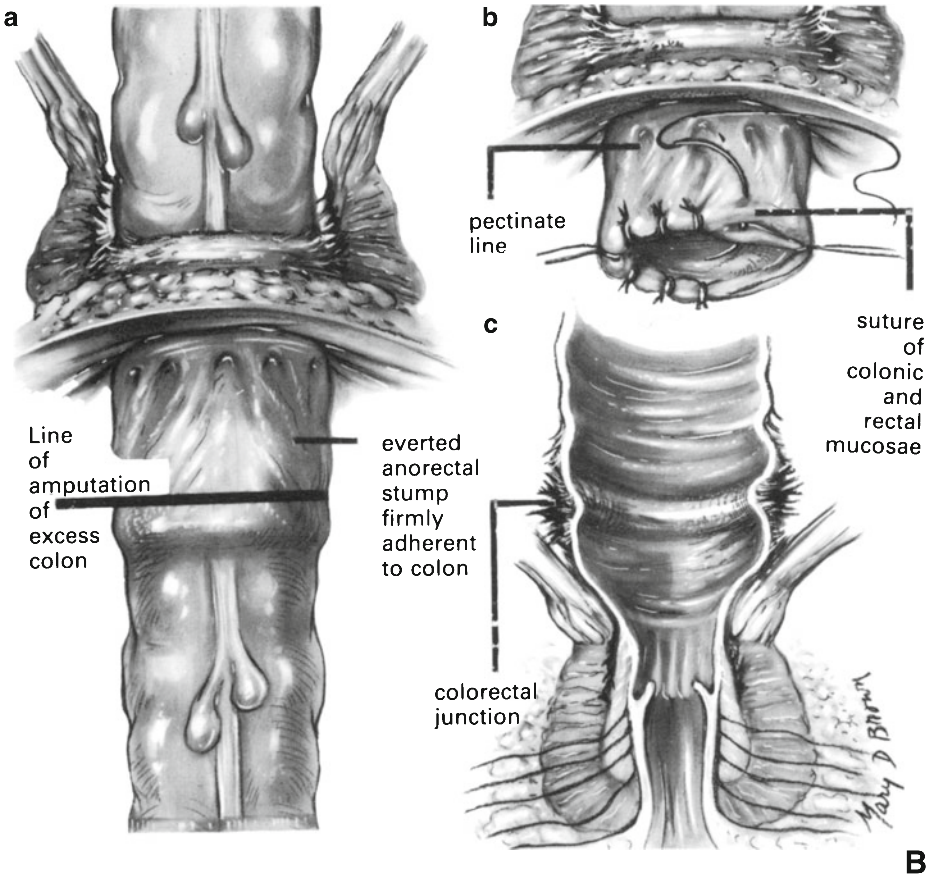


Fig. 5 (*continued*)

The validity of the long-standing opinion that a distal safety margin of at least 5 cm was required was seriously doubted only at the start of the nineteen-eighties in studies published by Hughes et al. (1983), Williams and Dixon (1983) and Pollet and Nicholls (1983) [31]. These showed that distal intramural tumor spread is extremely rare, and also demonstrated that survival and recurrence rates are independent of the distal safety margin. Rigid application of the 5 cm rule was therefore abandoned and resection 2 cm below the distal tumor margin was deemed adequate [32]. This extended the spectrum of indications for sphincter-preserving anterior rectal resection to cancers of the middle and lower third of the rectum as well.

Further notable innovations were improvement of the oncological outcome by consistent application of so-called total excision of the mesorectum, which involves resection along pre-given anatomical structures [33] and improvement of the functional outcome by the creation of a reservoir.

Schiessel (Fig. 7) introduced further advancements of intersphincteric resection in 1984. The technique was performed simultaneously by two teams, one from abdominal and the other from the perineal approach, in the Lloyd Davis position. Furthermore, resection of the rectum was extended into the intersphincteric gap, and the internal sphincter muscle was resected either completely or partly as a continuation of the rectal wall. The resection technique was identical with abdominoanal resection: complete mobilization of the rectum to the pelvic floor, and inclusion of the mesorectum. The concept of the hand-sutured coloanal anastomosis with the use of a protective transversostomy was also established. The method was used in patients with stage T1 to T3 or T1 or G2 tumors. Preliminary results were published in 1994; the technique was used in 38 patients. A local recurrence rate of 8% was observed [34]. Long-term results were published in 2005, with a median follow up of 72.86 months ($n = 117$) [35]. In the latter study 5.3% of patients developed local recurrence.

Braun and co-workers reported a series of 63 patients with cancer of the lower third of the rectum who underwent intersphincteric resection according to Raguse et al. 's technique, using a sutured or stapled anastomosis between the colon and the everted anal canal; a

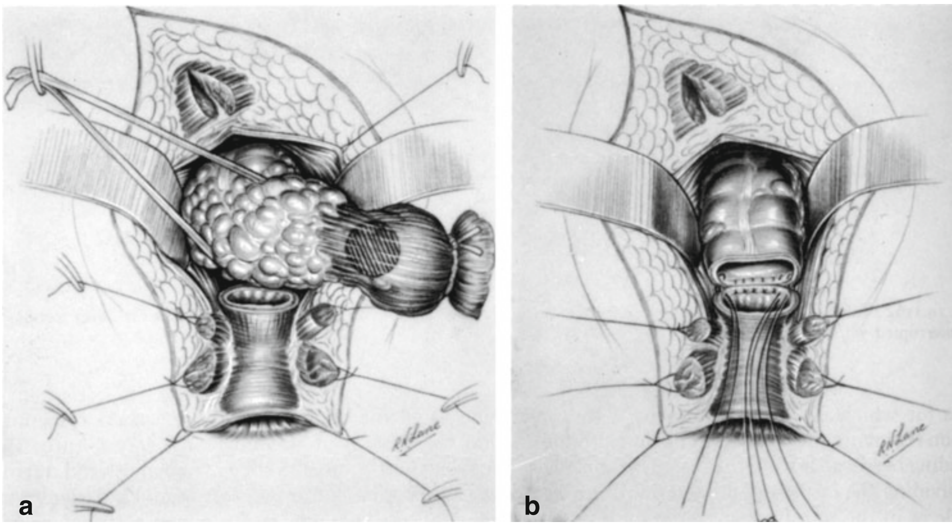


Fig. 6. Fig.19.117. page 690: The abdomino-transsphincteric resection. Transsphincteric phase with the patient in prone position. The levator and external sphincter have been divided to expose the lower rectum. (**a**) The rectal tube has been divided transversely close to the top of the internal sphincter and the colon is being drawn down. (**b**) The segment of rectum containing the growth and the distal part of the left colon have been resected and an end-to-end colorectal anastomosis in one layer is being made. (from John Goligher, Fifth Edition 1983, Surgery of the Anus, Rectum and Colon; Elsevier Verlag, published by Bailliere Tindall, London)

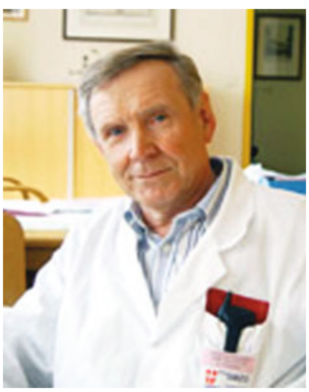


Fig. 7. Rudolf Schiessel, Vienna

mortality rate of 6% was observed. In a follow-up period of 6.7 years, 11% of patients experienced local recurrence. Continence was deemed perfect in 80% of patients [36, 37].

Rullier was the first who realized that intersphincteric resection is an excellent method for using a combined laparoscopic-peranal approach [38]. TME is performed here by the laparoscopic method. The specimen is obtained transanally.

Intersphincteric resection is a valuable procedure for sphincter-saving rectal surgery. The development of the operation technique for rectal cancer has a long history. Essential factors for a good result with this technique are proper preoperative planning and an atraumatic surgical technique.

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Surgical technique of intersphincteric resection

Rudolf Schiessel

Introduction

Sphincter saving surgery of rectal cancer has made an enormous progress over the last 50 years. Pioneers such as Hochenegg [1], Mandl [2], Finsterer [3], Dixon [4], Cutait [5], Bacon [6], Goligher [7], Parks [8], Nicholls [9], Heald [10] and many others have contributed in different ways to this development. The awareness that the lymphatic spread of this tumor occurs only in oral direction within the mesorectum and the local spread is only a few millimeters in distal direction opened the chance of sphincter salvage even in tumors close to the sphincter apparatus. Such tumors had been treated traditionally with abdominoperineal resection. But as long as the sphincter apparatus is not infiltrated by the tumor, there is no reason to remove the sphincter with all its unpleasant sequelae for the patient. Since we have nowadays excellent tools to exclude sphincter infiltration preoperatively we are able to plan these operations properly.

In order to remove tumors of the lower rectum close to the sphincter we have developed a technique whereby an abdominal part and a perineal part as well is performed. The basic idea of this procedure is to have a maximum exposure of the lower part of the rectum and the sphincter apparatus without damage to the sphincter muscle. Since the lower pelvis is a narrow funnel the dissection in this area can be extremely difficult. In the past, several approaches have been used to expose the lower rectum properly. For some time the abdominosacral way seemed to be promising for this purpose [11], but received no wide acceptance. Another approach was the transsphincteric route with transsection and reconstruction of the sphincter apparatus [12]. In addition the transanal route was in use for some time [8]. After having used the above approaches the intersphincteric route has become in our hands the favourite route to deal with tumors of the lower rectum not accessible from the abdomen alone [13]. There is no question, that in some females with a wide open pelvis low tumors can be resected from the abdominal route without an additional perineal part.

The following chapter will describe our technique in detail:

- Indications
- Diagnostic procedures
- Instruments
- Positioning of the patient
- Positioning of the surgical team
- Surgical technique
- Postoperative care
- Results

In this chapter we describe our technique of intersphincteric resection (ISR). This technique has been developed over a long time period. The oncological and functional results and the postoperative complications as well have been evaluated in a strict follow up program.

Indications (Fig. 1)

ISR is an alternative to abdominoperineal resection for cancers of the lower third of the rectum. The lower third of the rectum is defined by the "rule of four" as the region from 4–8 cm from the anus. Since the anal canal measures in many people less than 4 cm, the lower third will be then eventually 2–6 cm from the anus. Usually such tumours can be reached by the finger and are accessible for a clinical staging. Even extensions into the anal canal are no contraindication, provided they are superficial.

ISR is a useful operation for big villous adenomas even when they reach into the anal canal. We have used it also for low carcinoids and hemangiomas. New indications are residual tumours after mucosectomy for superficial cancers and after radiotherapy.

The operation is not indicated in undifferentiated cancers, in the presence of sphincter infiltration, in a T4-stage and when sphincter function is insufficient.

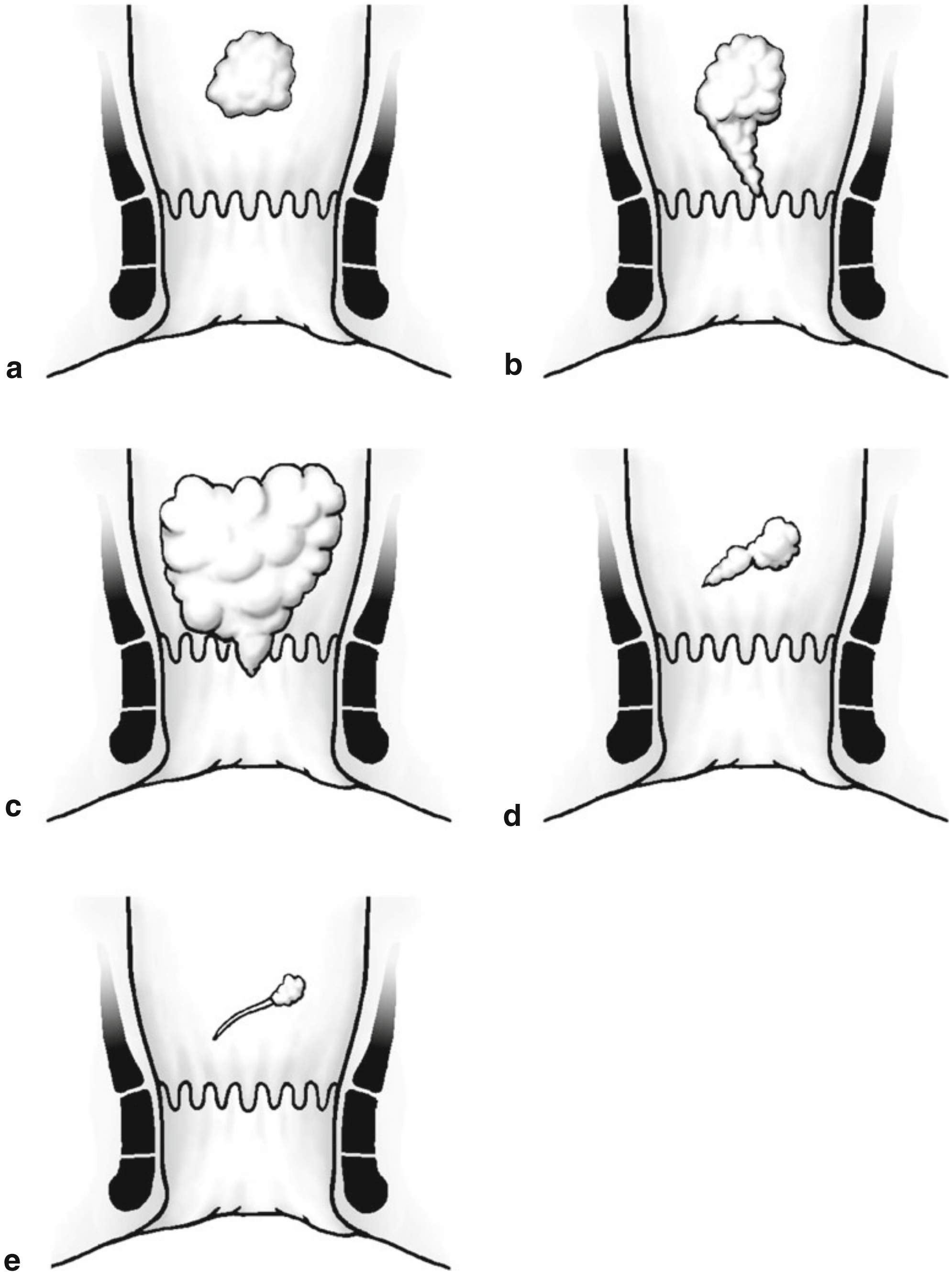


Fig. 1. Indications for ISR. (**a**) Tumor in the lower third of the rectum; (**b**) Tumor with extension into the anal canal; (**c**) Large villous adenoma; (**d**) Residual tumor after endoscopic mucosectomy for early cancer; (**e**) Residual tumor after radiotherapy

To perform this operation not only the knowledge of the surgical technique, but also a proper preoperative planning is important. ISR is not a standard operation for rectal cancer.-It is only indicated in tumors of the lower third of the rectum. Thus we have to collect many informations before we proceed with surgery.

Diagnostic procedures

Endoscopy and biopsy

Most patients will already come with the report of a coloscopy or rectoscopy. When we check the report we have to look if there is any information about the distance of the tumor from the anus. Most non-surgeons will make no documentation of the exact localization of the tumour. Another problem is that coloscopes have the first distance marks beyond 10 cm. Therefore it is sometimes necessary, that the surgeon performs a digital exploration and a re-endoscopy of the lower rectum as well. There are several questions to answer: how far is the tumour away from the sphincter, are there extensions into the anal canal, is the tumor mobile or fixed, does the tumor cover the entire circumference or only a part? What do we know about the other parts of the colon? Another important point is the histology report. We know, that undifferentiated cancers should be excluded from ISR. Although it is difficult for the pathologist to report the histologic grading from biopsies, it is useful to exclude any doubts by personal contact.

Magnetic resonance imaging

Sphincter saving surgery for tumors of the lower rectum is dependent on the fact that the sphincter apparatus is not infiltrated by the tumor. Another important issue is the circumferential tumor free margin. The close proximity of vagina, prostate, urethra and urinary bladder needs a careful evaluation in their relation to the tumor. MRI has been shown to provide a good preoperative information concerning sphincter infiltration and prediction of a circumferential tumor free margin. The excellent quality of modern MRI provides a good road map for the surgeon. In case of a circumferential tumor free margin of less than 1 mm a neoadjuvant radio-chemotherapy is advisable.

Endosonography of the rectum

This is an excellent method for the local staging of rectal tumors. We prefer rectal MRI because of a long experience and a good cooperation with our radiology team.

Other imaging

In order to exclude metastases to the liver an ultrasound is sufficient. An X-ray to the chest is mandatory.

Sphincter manometry

Sphincter saving procedures are based on the hypothesis, that the sphincter to be saved works properly. With a careful history and digital examination we can exclude severe cases of faecal incontinence. Sphincter manometry gives an objective information about sphincter function and will help in difficult decisions. It should be mandatory in studies evaluating the results of ISR.

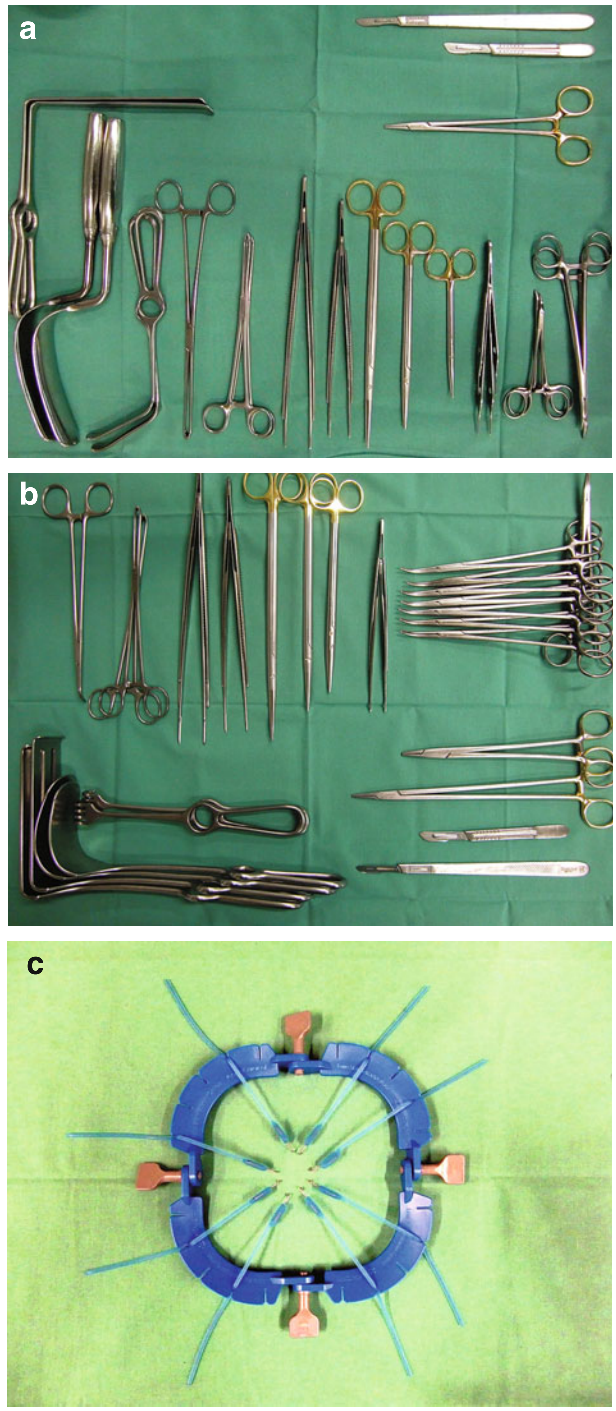


Fig. 2a–c. Instruments for the abdominal and perineal part

Planning of surgery

After having collected all above informations, we have to decide as to whether we proceed with surgery or we need a down staging of the tumor in order to facilitate sphincter salvage without the danger of local recurrence. Routine use of neoadjuvant radiation or radio chemotherapy is not justified because of its eventual side effects, in particular on bowel function. Tumors with an estimated circumferential tumor free margin of less than 1 mm in the preoperative rectal MRI should undergo neoadjuvant treatment.

Preoperative planning has to involve the patient and her or his relatives. We should explain the chances of cure from the cancer and the possibilities of treatment. It is important to mention, that the salvage of the sphincter does not mean that bowel function will be completely normal after surgery. The loss of the ampulla recti as a reservoir and a possible weakness of the sphincter need to be explained, otherwise the expectations of the patients will be too high. We made the experience, that the better people are prepared before the operation, the higher is the degree of satisfaction postoperatively even when functional problems occur.

The operation

Instruments (Fig. 2)

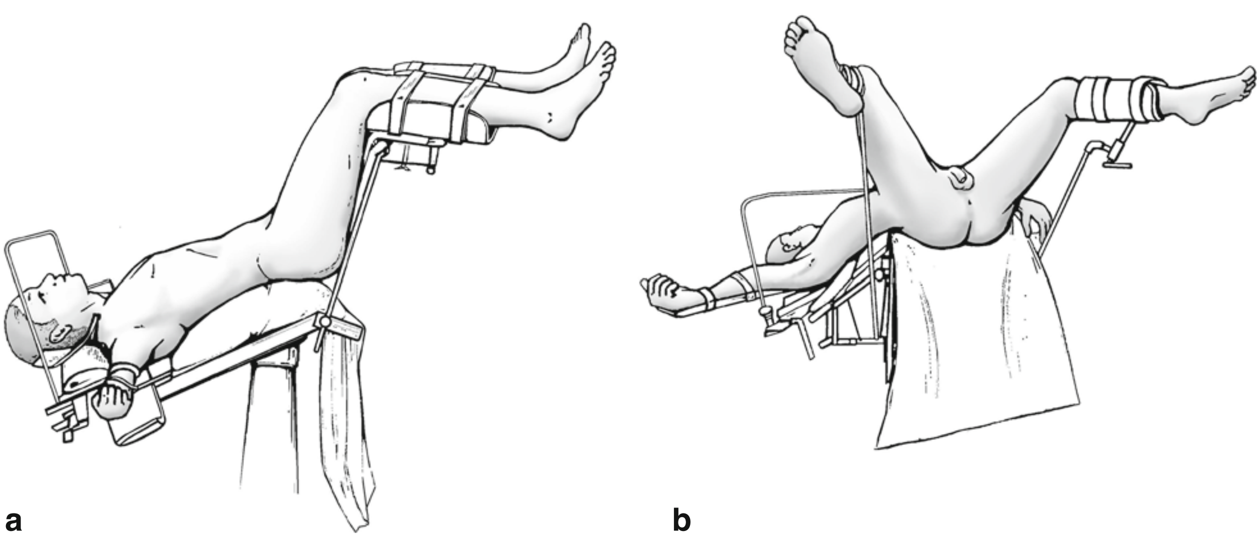
In general we need 2 sets of instruments: one set for the abdominal part of the operation and one for the perineal part.

For the abdominal part we need a typical set which can be used for all kinds of abdominal surgery. Important supplements are a self-retaining retractor and long blades of 25 cm in length or longer in order to expose the structures in the lower pelvis even in very obese patients. For haemostasis we use Ligasure or Ultracision with equal effect. Both instruments are also very useful for mobilisation of the mesorectum. Clamps, forceps and needle holders should have a minimum length of 25 cm.

For the perineal part we need a smaller set of instruments similar to that for the perineal part of the abdominoperineal resection. An important tool for the exposure of the anal canal is the Lone-Star retractor. This disposable set allows a atraumatic dilatation of the anal opening. Metal retractors are more traumatic and might damage the external sphincter. For entering the intersphincteric space we use small angulated Langenbeck retractors (135°). After entering the lower pelvis we use narrow blades of 10–15 cm in length.

Positioning of the patient (Fig. 3)

The Lloyd-Davis position should be facilitated on a modern operation table, where lifting and lowering of the leg supports is possible by a remote control. During the initial stage of the abdominal part a flexion of the hip joint of 20–25° is sufficient. As soon as the perineal team starts, the flexion should be changed to 80–90°. During the perineal part it is helpful to move the table from a horizontal postion to a 10° head down (Trendelenburg) position. Care has to be taken, that movements of the table or leg supports do not cause unphysiological pressures on nerves, skin etc. Therefore the movements and their effect on the patient should be checked before the patient is completely covered with sterile surgical drapes. Known



a b

Fig. 3. Positioning of the patient. (a) Lateral view: the leg supports should be attached to a mobile part of the table which can be moved by a remote control; (b) The buttocks should be positioned as shown here

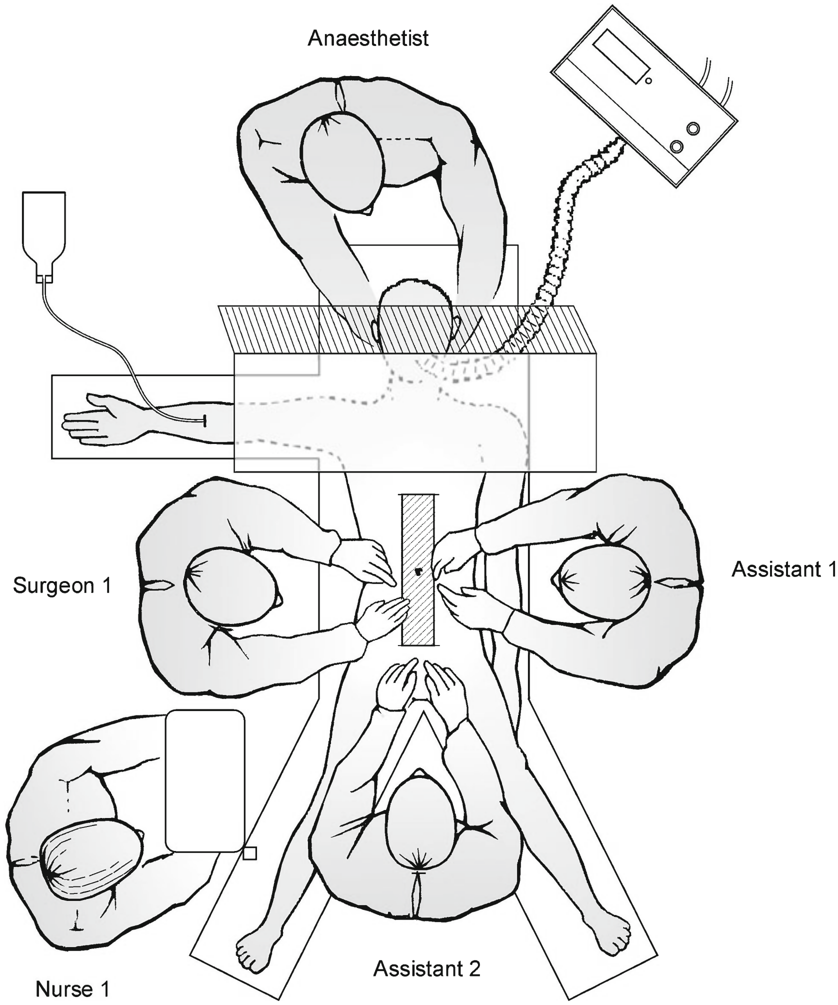


Fig. 4. Positions of the surgical team during the abdominal part

problems with the hip or knee have to be taken into consideration.

Positioning of the surgical team (Figs. 4 and 5)

The surgical team consists of 2 surgeons, 2 assistants, 2 nurses and 1 anaesthetist. Two additional people are necessary for support: one technician and one nurse. The abdominal surgeon starts with one nurse and two assistants. After full mobilization of the rectum the operation is continued by a synchronous approach to the lower rectum. The perineal surgeon starts with one nurse and one assistant.

Surgical technique

As mentioned above ISR consists of an abdominal part and a perineal part. In our experience it is recommendable to start with the abdominal part. The perineal part can be started as soon as the anatomical situation in the abdomen is clear and the rectum is mobilized as much as possible. From this point the operation is carried out as a synchronous abdominoperineal procedure.

Abdominal part

We open the abdomen from a midline incision from the umbilicus to the symphysis. In very obese patients or difficulties in mobilizing the left colonic flexure we do not hesitate to extend the incision.

After complete exploration of the abdomen we mobilize the sigmoid colon and identify the left ureter. Then we mobilize the left colon completely up to the left flexure. The next step is the incision of the pelvic peritoneum in the level of S_1. This can be done either on the left side of the rectum or on the right side. With traction on the rectum off the sacrum and blunt dissection through the opening in

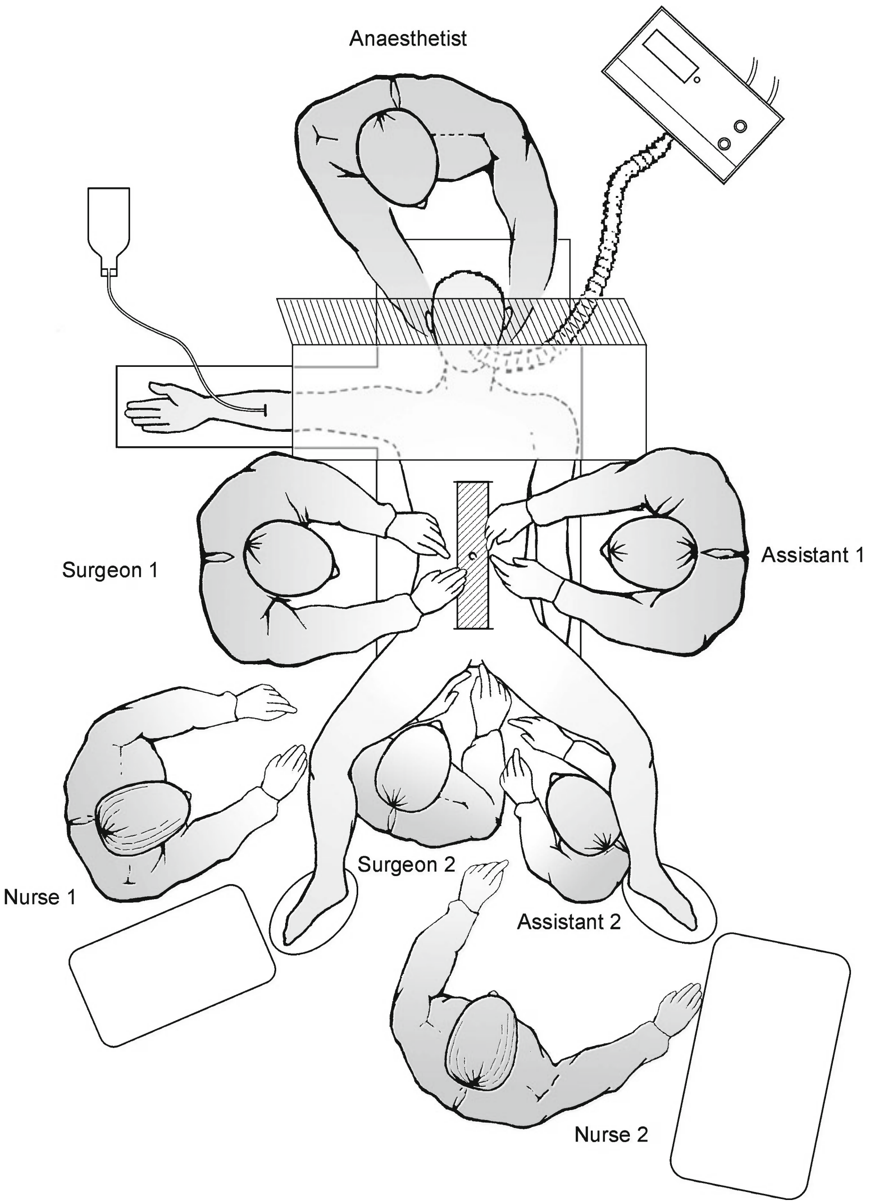


Fig. 5. Positions of the surgical team during the abdominoperineal part

the peritoneum the fascia of Waldeyer can be identified as thin transparent layer covering the sacrum and the hypogastric nerves (Fig. 6). As soon as they are identified we continue to mobilize the mesorectum by using Ligasure, Ultracision or diathermy. Currently we do not use unipolar diathermy in the lower pelvis any more in order to avoid a possible collateral damage to the pelvic nerves. When we are in the correct plane, complete dorsal mobilization of the rectum down to the pelvic floor is easy. After incision of the pelvic peritoneum on the ventral circumference of the rectum we start the identification of the fornix vaginae or the seminal vesicles. These structures are lifted off the rectum by gentle traction and dissection. Extreme caution is advisable to avoid damage of the branches of the autonomic nerve system. After the lower part of the rectum is mobilized dorsally and ventrally the lateral ligaments with the middle hemorrhoidal artery can be divided. Usually it is a small vessel that can be coagulated by Ligasure or Ultracision. In a next step the lower rectum can be mobilized down to the levator ani muscles. This is the point where the perineal team can start (see below).

The abdominal team continues with ligating the inferior mesenteric artery. It is advisable to check the collateral flow to the descending colon and sigmoid before cross clamping of the vessel close to the aorta. Sometimes it is necessary to clamp the artery beyond the branching of the left colic artery. A lymphadenectomy of the stem of the

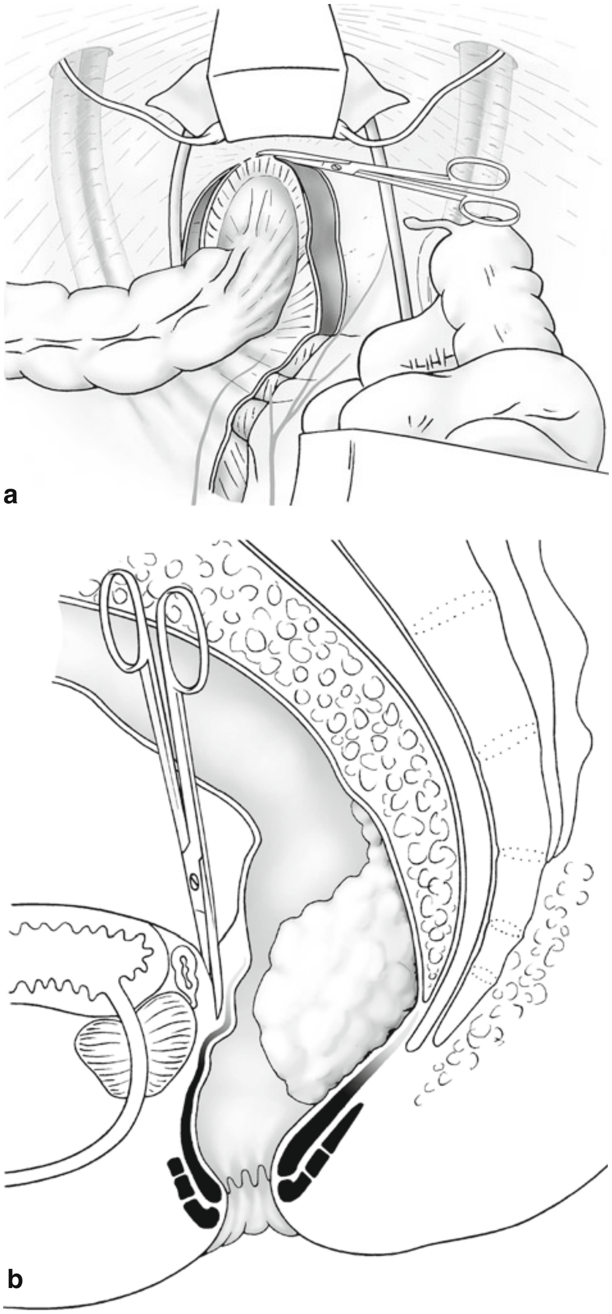


Fig. 6. Abdominal part: opening the pelvic peritoneum and entering the avascular plane between the mesorectum and the fascia of Waldeyer (**a**) and Denonvillier (**b**)

inferior mesenteric artery down to the aorta should then be performed. It is noteworthy that the hypogastric nerves can be damaged in this area. The next step is the decision where to divide the sigmoid colon. Before we make a definitive decision, the blood supply should be checked. For oncological reasons it is not necessary to remove more than the rectum and mesorectum for a tumor located in the lower rectum. Thus we should not resect too much colon, provided that its blood supply is warranted, in order to have enough colon for reconstruction. Division of the colon is usually performed using a linear stapler. The vascular pedicle is then formed starting from the divided inferior mesenteric artery and continuing to the section line of the colon. After full mobilization of the sigmoid and descending colon we get an estimate of the available length for reconstruction. For a coloanal anastomosis the colon should reach without tension 5 cm beyond the symphysis. The operation is continued with stepwise approaching the lowest part of the rectum and so coming in close contact to the perineal team. It is very useful for the orientation in the lower pelvis and the management of difficult situations, when the dissection in this area is carried out synchronously. As soon as the tumor bearing rectum is completely mobilized, the specimen is delivered transanally. After delivery we recommend an immediate inspection of the specimen on a separate table to check whether the resection of the tumor has been sufficient. It is optimal to do this in the presence of a pathologist.

The final step of the abdominal team is the construction of a protective stoma. Although there is no proof that a stoma is really necessary, we have performed it in all our cases. Depending on the anatomical situation we perform either a transverse colostomy or an ileostomy. A presacral sump drain is introduced before the abdomen is closed.

Perineal part

This part is very much dependent on a good positioning of the patient. The legs have to be lifted from a Lloyd-Davis position to almost lithotomy position, taking care that the abdominal team is not disturbed.

When the anal region is well exposed, the Lone-Star retractor is inserted. We use always 8 hooks in order to have a good approach to the anal canal and lower rectum.

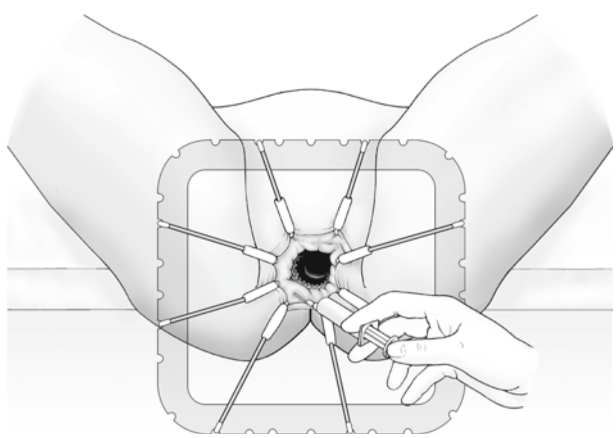


Fig. 7. Perineal part: infiltration of the perianal skin with a diluted adrenaline solution

Low tumors are now visible and their effective distance to the sphincter apparatus can be determined. The next step is a subcutaneous infiltration of the anal skin with an epinephrine solution of 1:200.000 in order to have a dry operative field during the dissection (Fig. 7). Thereafter a circular incision is made above the internal sphincter. The underlying sphincter is identified as a white band of about 3 mm in thickness (Fig. 8a). We lift the muscle fibres with a forceps so that we can enter the intersphincteric plane (Fig. 8b). With gentle dissection the external sphincter, which has a reddish appearance, can be separated. As soon as a good dissecting plane is achieved the internal sphincter is mobilized in the entire circumference (Fig. 8c). Following the intersphincteric plane we approach the lower pelvis and get in touch with the abdominal team. The lower rectum is now dissected off the Waldeyers fascia. The dissection in the anterior part of the lower pelvis follows the intersphincteric plane, taking care to

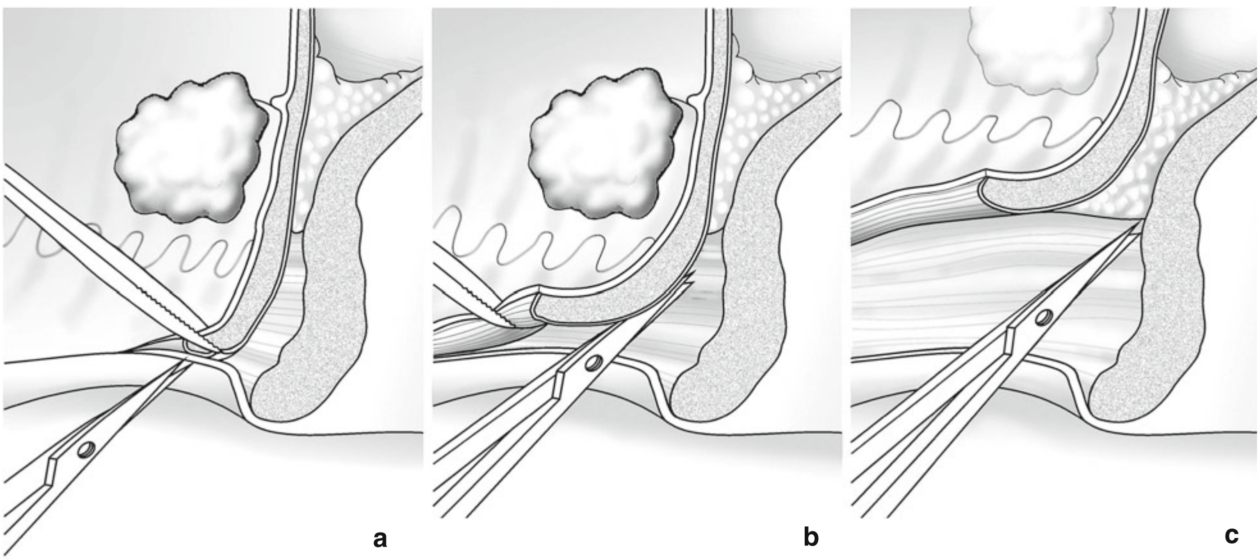


Fig. 8. Perineal part. (**a**) Identification of the internal sphincter; (**b**) Entering the intersphincteric space; (**c**) Circular mobilization of the internal sphincter

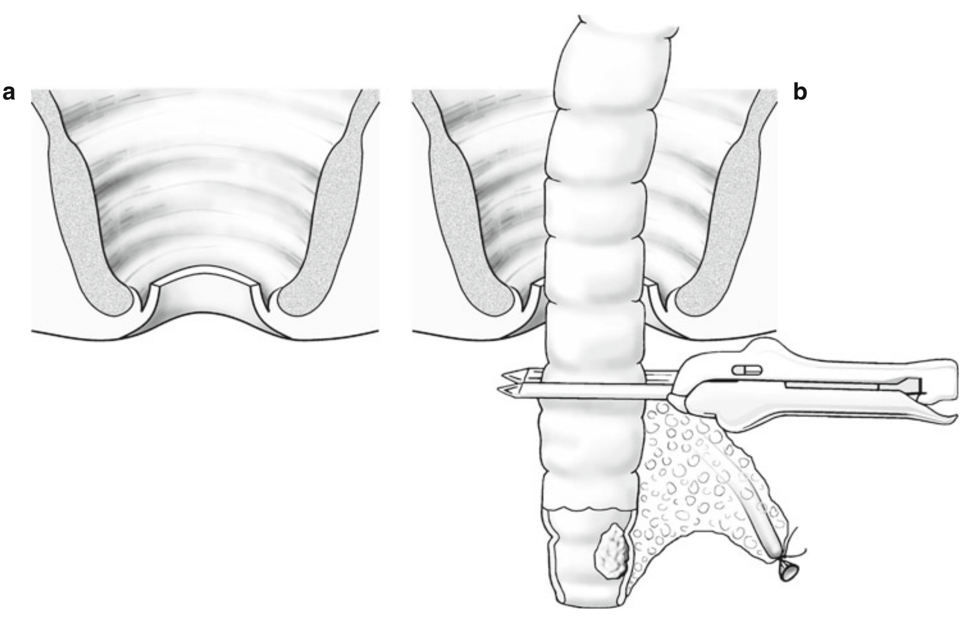


Fig. 9. Perineal part. (**a**) Anatomical situation after complete mobilization of the lower rectum and internal sphincter; (**b**) Transanal pull-through of the tumour bearing rectum and mesorectum. Transection with a linear stapler

avoid accidental injury of the male urethra, the vagina or prostate. In case of difficulties to finish the anterior mobilization of the lower rectum it is helpful to pass the divided rectum through the anal canal with its upper end. It is then much easier to divide final adhesions to the anterior rectal wall. After peranal harvest of the specimen (Fig. 9b) and its inspection (see above) a washout of the pelvis with saline solution is performed. This is followed by thorough inspection of the pelvis from above and from below for residual bleeding.

The final step is the reconstruction of the bowel continuity (Fig. 10). The decision has to be made as to whether a pouch is performed or not. This will depend on 1. the available length of colon and 2. On the volume of the mesenteric fat in relation to the capacity of the pelvis. The latter problem arises usually in obese men with a narrow pelvis. When possible, we perform a coloplasty pouch. An incision of about 5 cm is made along the taenia libera, this is closed then in transverse direction by a one layer (000) suture. Thereafter continuity is restored with a coloanal anastomosis. It is important to restore the anal canal and to avoid a mucosal prolapse. This can be achieved by putting the stitches first through the anal skin, then through the external sphincter and then through the full thickness of the colon. Before tightening the knots an exact adaptation of the mucosa to the skin is important. A release of the hooks of the Lone-Star retractor is helpful to get some skin into the new anal canal. When the anastomosis is finished, the retractor is removed. Contraction of the sphincter is usually observed after removal of the retractor.

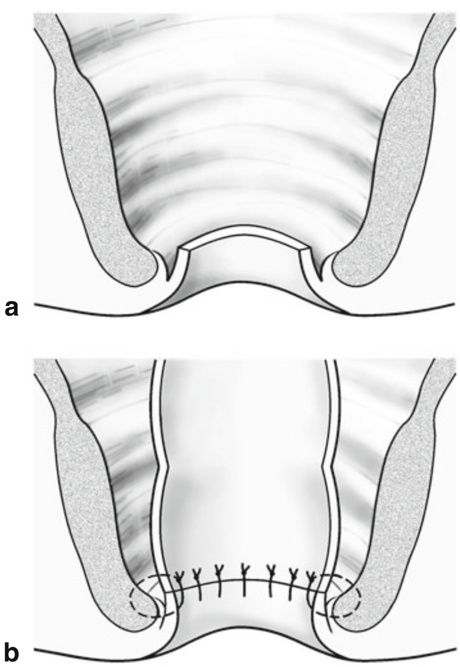


Fig. 10. Perineal part. (**a**) Preparation for intestinal reconstruction; (**b**) Coloanal anastomosis with reconstruction of the anal canal

Fig. 11. Postoperative check of the coloanal anastomosis with water soluble contrast medium

Postoperative care

Patients are mobilized on the first day after surgery or on the evening of early morning surgery, depending on their physical condition. A careful pain management is important. Oral fluid is allowed as soon as full consciousness is achieved after anaesthesia. Breathing exercises are also necessary. Food is usually tolerated from day 2 after surgery. Discharge from hospital is possible from day 7, depending on a good organized home care including stoma care.

Six weeks after surgery we check the coloanal anastomosis and the pouch by digital palpation and by an X-ray with a water soluble contast medium, introduced via the protective stoma (Fig. 11). This is done in order to exclude fistulas. In case of a perfect result we check the sphincter function with a manometry. In case of low sphincter pressures we start a biofeedback training immediately. Provided that the healing process and sphincter function are satisfactory, the stoma can be closed.

Results

From 1984–2009 a total of 265 patients has been operated on with intersphincteric resection. In a long-term study 149 patients until 2005 were evaluated [14].

Over this long period the surgical technique and the preoperative evaluation have been improved. Major prog-

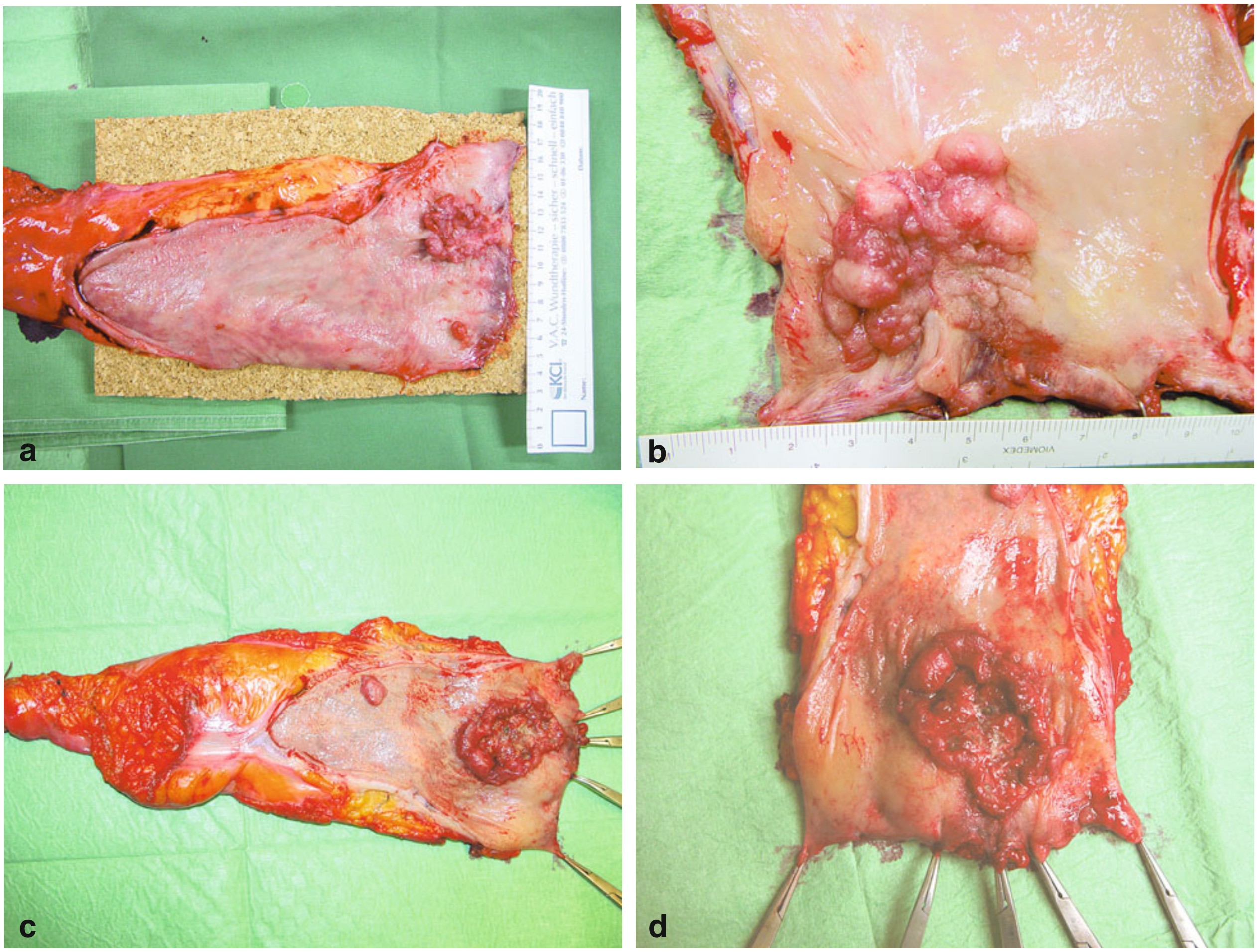


Fig. 12a–d. Specimens of patients after ISR. Note that most tumours reach up to the dentate line

ress has been made in the atraumatic treatment of the sphincter apparatus by changing from the Parks-speculum to the Lone –Star retractor. Another improvement was the modification of the coloanal anastomosis in order to reconstruct the anal canal with fixation of the anoderm to the original level inside the anus. This avoids mucosal prolapse with leaking of mucous and improves anal sensation. Haemostasis has been improved by applying less monopolar diathermy and more Ligasure or Ultracision. The preoperative evaluation was improved significantly by the introduction of rectal MRI in 1996. The preoperative interdisciplinary workup of the MRI images together with the other informations (endoscopy, histology, sphincter manometry etc.) allowed a better selection of the patients suitable for ISR.

Indications

The majority of our patients had low rectal cancer (Fig. 12). The median distance from the anus was 3 cm, measured with a rigid sigmoidoscope. Other tumors were large villous adenomas and carcinoid tumours.

Complications

Early complications occurred in 10 patients. One patient died from pulmonary embolus. Two needed relaparotomy because of haemorrhage and a small bowel fistula. Seven patients developed a fistula from the coloanal anastomosis, which was treated with a delay of closure of the protective stoma in 6, but one needed re-resection because of intestinal-urinary fistula.

Late complications comprised a small bowel obstruction, one fistula after stoma closure, which healed spontaneously and 11 strictures of the coloanal anastomosis. These could be treated by repeated dilatations in all cases. For this purpose we used Hegar-type metal dilatators. Dilatations did not need general anaesthesia and were performed in the outpatient department.

Oncological results

In a very careful prospective follow up study 113 patients with curative ISR for low rectal cancer were traced up to 16 years. During this long period we observed 6 local recurrences (5,3%). Fourteen patients died from cancer, the mean overall survival was 126 months.

Functional results

The continence function was evaluated according to the scoring system of Williams and Johnston. Continence for solid, liquid stools and gas was achieved in 86% of the patients. Continencenly for solid stool was observed in 13%, incontinence in 1%. Anal manometry showed a decrease in the resting pressure and the squeeze pressure as well after ISR. The resting pressure remained low over the observation period, but the squeeze pressure recovered to nearly normal values (Fig. 13). The surprisingly good functional result concerning the sphincter might be explained by the improvements in the surgical technique, the biofeedback training before stoma closure when necessary and a qualified postoperative care in a follow up clinic.

Many patients experienced a high stool frequency within the first months after closure of the protective stoma. The situation improved considerably after six months. After 2 years the median stool frequency per day was 2,3 (Fig. 14). In order to improve the reservoir function of the neorectum we constructed a colon pouch when possible. We found it in most cases impossible to construct a J-pouch, either because of a bulky mesenterium or because of inadequate length of bowel. Therefore was our preferred pouch a coloplasty pouch. Since this was not performed within a randomized trial, it is difficult to recommend a pouch construction on principle.

The problem with high stool frequency can be treated with Loperamide. In case of unsatisfactory bowel function it is important to exclude strictures of the coloanal anastomosis or neorectum. A sphincter manometry helps to exclude insufficient sphincter function.

Dissatisfaction with postoperative function after ISR is very rare. In our experience no patient required a stoma because of fecal incontinence or other functional problems.

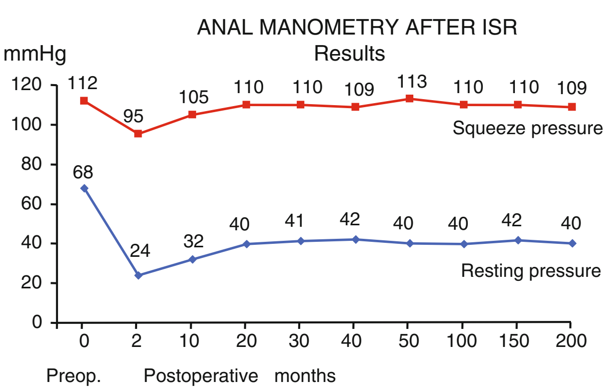


Fig. 13. Long-term results of sphincter manometry

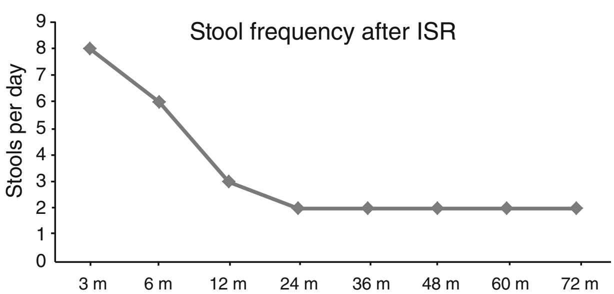


Fig. 14. Long-term results of number of defecations per day

Conclusion

Intersphincteric resection expands our possibilities of sphincter salvage to tumours located in the lower part of the rectum. It is not in competition with the standard procedures such as anterior resection. Careful planning, proper selection of cases and an atraumatic surgical technique are the prerequisites for a good long-term result.

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The laparoscopic technique of intersphincteric rectum resection

Peter Metzger

The current treatment of rectal cancer involves a multidisciplinary approach in order to achieve three primary goals

1. Curing cancer with a radical resection and minimizing the local recurrence rate while optimizing the chances for achieving the primary goal: a best oncologic outcome.
   This requires:
   (a) Total mesorectal excision (TME) with autonomic nerve-sparing for rectal cancer has been proven in various studies.
   (b) Patients with T3 disease, with infiltration of the mesorectum or internal sphincter and/or with preoperative N+ staging may receive preoperative radio chemotherapy to obtain down staging.
2. Optimizing the patient's quality of life for most cases with a sphincter-saving procedure even in the lower third by an intersphincteric resection with coloanal anastomosis.
3. The laparoscopic approach may have advantages over the conventional technique: fewer traumas to the abdominal wall, less pain, shorter hospital stay and good cosmetic result.

Introduction

Eighteen years after the first report [1] of laparoscopic colorectal surgery, the spotlight has drifted from technical feasibility to oncologic adequacy in cancer. The feasibility of laparoscopic surgery for rectal cancer in expert hands has been demonstrated in the literature [2, 3].

Laparoscopic rectal surgery has been proven to be oncologically equivalent to conventional surgery, but the resection for cancer is more complicated than laparoscopic colectomy for benign disease. This technique has been shown to be safe and oncologically equivalent to conventional surgery.

Scepticism prevails in laparoscopic resection of rectal cancer, in particular sphincter-preserving resection for low and very low rectal cancer. Laparoscopic resection of very low rectal cancer must also conform to the current standards in rectal cancer surgery. The procedural complexity has limited the widespread application of laparoscopic sphincter-preserving technique.

For the lowest of rectal cancers, the final technique for sphincter-preserving resection is an intersphincteric proctectomy with colo-anal anastomosis [4].

The key concept in pushing sphincter preservation forward has been the realisation that the circumferential margin is all-important, but unless the rectal tumour involves the external sphincter muscle, there is no oncologic need to remove it, and the APR is not necessary and the continuity of the gastrointestinal tract can be restored.

As stated above, from a historical standpoint, the critical issue in low rectal cancer surgery has been the distal resection margin. The crucial question has been: at which level in the lower rectum is a patient a candidate for a sphincter saving resection? How low can we go with the resection line, with the oncological radicality without a risk of R1 resection? The "classical" five centimeter rule was founded in hesitation, in the fear of local recurrence. If one accepts the 2-cm rule as an adequate distal margin, the more patients will be operated on with a low anterior resection, but most patients with tumours close to the anorectal ring would not be treated with this technique.

It was demonstrated by many authors that even a distal resection margin of 1 cm or less may be sufficient in radical attempts of sphincter preservation for the lowest positioned kind of tumours [5]. In many recent publications in about 4–5% of the cases there may be intramural tumor cell spread distal to the tumour of <1 cm. The distal resection margin does not predict local recurrence. This postulate was the oncological basis for the idea, that the preservation of the sphincter apparatus may be possible, also from an oncological perspective.

In summary, when the muscles of the pelvic floor and external sphincter are not infiltrated by tumour cells, their removal is not indicated. The highest risk after low rectal resection may be the local recurrence in the pelvic area. This can be caused either by a distance from the distal or circumferential resection margin.

Intersphincteric rectal resection is chosen for patients with tumours that are located in proximity, either just above or extending, in to the anal canal but which have not invaded the external sphincter muscle or pelvic floor.

Laparoscopic technique for intersphincteric rectal resection

Advantages

1. The laparoscopic approach offers some potential benefits over open surgery, such as earlier return of bowel function, fewer hernias, reduced postoperative pain, shorter hospital stay and a better cosmetic result.
2. The introduction of laparoscopy into the low rectal cancer surgery in the past decade has helped to get a better view on the detailed anatomy of the lower pelvis due to the magnified and clear view using the HD laparoscopy. Through this technique it is easier to identify the Denonvillier's fascia, and save the autonomic nerves, to evaluate cancer invasion into the seminal vesicle, prostate or vaginal wall. Magnified view obtained by laparoscopy provides a more precise image of the dissection plane covering the mesorectum and makes the preservation of the pelvic autonomic nerves easier even in a narrow pelvis.
3. The laparoscopic HD camera gives us in the lowest part of the pelvic floor an excellent and enlarged view. Also the exact preparation and dissection in the correct planes is easier with the laparoscopic technique. We have for this part of the procedure a bright and sharp picture and have a good view also of the dorsal part of the vagina or prostate, better then by the conventional, open operation.
4. With the laparoscopic technique it is possible to perform the dissection towards the intersphincteric space and the connection with the transanal intersphincteric dissection ("rendezvous technique").

Disadvantages

1. The mobilisation of the left colon, including the sigmoid colon, and the mobilisation of the splenic flecture is a very easy and standardised technique for an experienced laparoscopic surgeon, but can be very difficult in obese patients and after prior laparotomy. It is a hotly disputed question, whether the mobilisation of the splenic flexure is necessary in all cases or not?
2. One of the most significant advantages in the treatment of low rectal cancer has been the concept of total mesorectal excision (TME), but the laparoscopic preparation can be technically very difficult in the pelvic floor. Despite the procedural complexity, some studies have reported a laparoscopic approach for total mesorectal excision with sphincter preservation.
3. Location of the tumours. Since palpation is not possible during laparoscopy, the exact localisation of the tumour is not possible. Sometimes it is wise to make a preoperative tattoo with black ink into the rectal wall with a coloscope.
4. A great discrepancy between a small diameter of the pelvic floor and the bulky tumour, or an extremely ventral curvature of the sacrum can be also a great challenge for the laparoscopic technique.

In order to avoid the above problems we developed a new technique for laparoscopic intersphincteric rectum resection, by which two teams are working in parallel from the abdominal and perianal side.

Indications – contraindications

The decision to operate on a patient with a very low rectal malignancy should be based on the surgeon's expertise in laparoscopic and also in low rectal cancer surgery. Please do not forget: a conversion to the open technique should never be viewed as a fiasco, when patients' safety has to be protected.

The indication for laparoscopic intersphincteric resection for a very low rectal cancer does not differ from those to the open technique. Careful patient evaluation must be for done in candidates for laparoscopic ISR. Preoperative tumour evaluation is critical when considering a laparoscopic approach to rectal cancer.

Laparoscopic ISR has been proposed to offer sphincter preservation in patients with very low rectal cancer without tumour-infiltration into the external sphincter muscle, including T1–T3 tumours, but not G3 and also not in patients with disturbed continence.

Bulky large tumours or evidence of adjacent infiltration of the external sphincter muscle or the intersphincteric space should be carefully analysed to decide whether laparoscopy is feasible. Helpful for this evaluation can be the MRI examination. This procedure is also very important after neoadjuvant chemo-radiotherapy.

Laparoscopic ISR is relatively contraindicated in patient with a volume incongruence between the diameter of the mesorectum and the diameter of the pelvic floor. The operation is also relatively contraindicated in a small and extremely curved pelvic floor.

After any open abdominal surgery a laparoscopic ISR can be very difficult or impossible, but also in such patients a pelvic MRI can be helpful for a better judgement of the situation.

Technical requirements

1. **Video-laparoscopic equipment**
   The best and optimal solution may be a High Definition (HD) Video "Tower" with two monitors, automatic insufflators with warmed CO_2 gas supply and possibility for video-documentation. A 30 degree optic lens is generally used.

2. **Patient-Positioning at the operating table**
   The patient's positioning is of paramount importance in case of rectal surgery. It must allow any two types of operation, planned while providing good facilities for the two stages – abdominal and perineal – particularly of a two teams procedure.

   The patient must be stably fixed, with the possibility in all time to move in all directions. Both shoulders have to be supported to preserve of stabile positioning.

   The operating table must have enough mobility to facilitate a head down and right- and left-sided positioning simultaneously. We use the system of Magnus 1180 (Maquet™, Germany – Fig. 1.) for the positioning of the patient on a vacuum mattres in order to achieve a stable fixation of the patient during movements of the operation table.

   The patient is placed in an exaggerated lithotomy position (Fig. 2).

3. **Positioning of the operation team and the laparoscopic video equipment**
   The main monitor is placed on the left side of the patient, at the hip level, and the secondary monitor is placed on the right side at the same level. The surgeon is standing on the right side of the patient, the assistants on the left side and the second assistant left from the first assistant. The nurse is placed to the right from the surgeon (Fig. 3).

4. **Laparoscopic instruments and preparations technique**
   The dissection in embryological planes can be undertaken in two modern, but essentially different ways. The first is based upon monopolar laparoscopic instrumentation (graspers, scissors, Hook-electrode) or bipolar diathermy (Ligasure™), second on Ultrasonic dissection. In our experience the Ligasure preparation is the standard technique, the optimal exposition of the complex anatomy of the depth of the pelvis is achieved by bipolar electrosurgery. In addition the dissection with traction and counter-traction (with the laparoscopic bowel clamps) is important as well.

   A special retractor for better exposure for laparoscopic preparation in the depths of the pelvis is not an obligatory tool, because the "classic" preparation

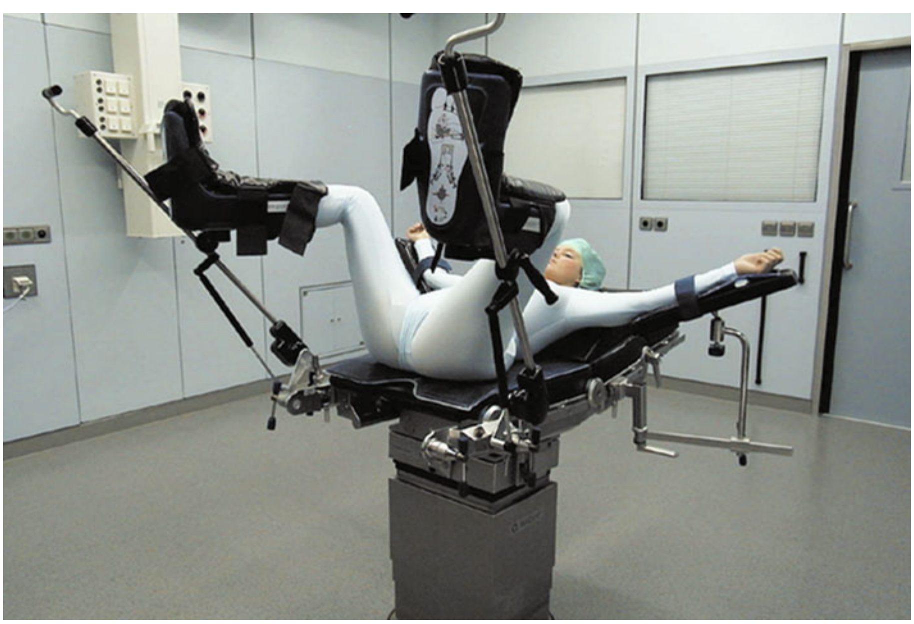


Fig. 1. Magnus 1180, Maquet™ operating table with special leg supports

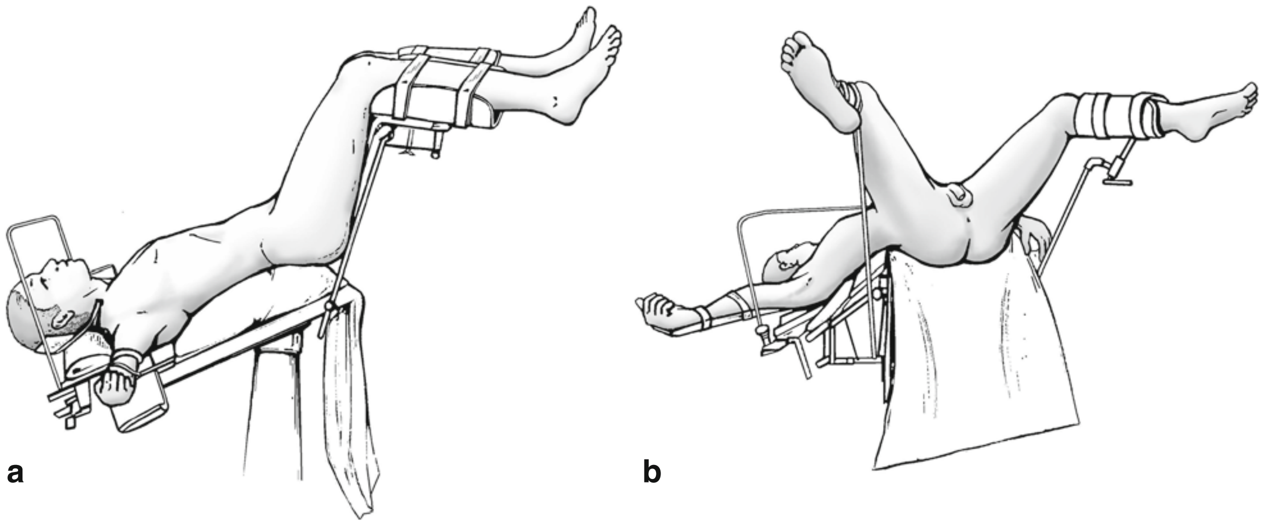


Fig. 2a, b. Patient-positioning: Exaggerated lithotomy position

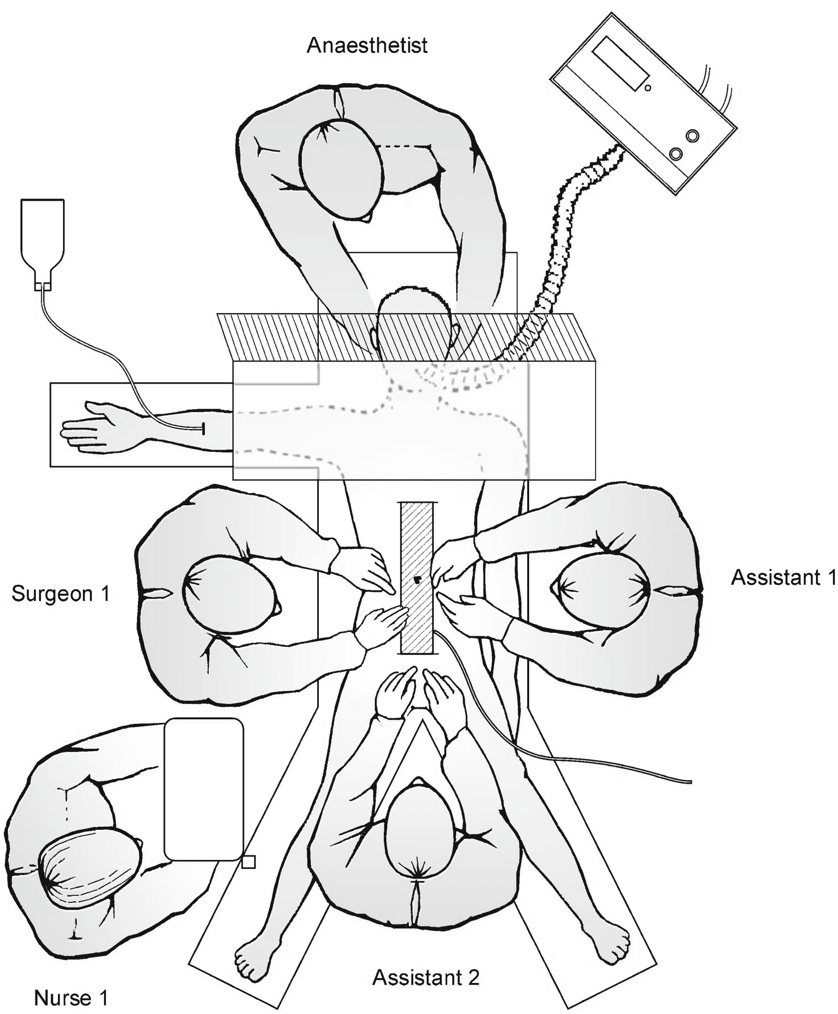


Fig. 3. Positioning of the operation team

technique for (traction – counter traction) can be applied with the help of the standard laparoscopic bowel clamps.

5. **Retraction of the specimen**
   After completing the circular intersphincteric dissection, the tumour – bearing rectum can be removed "en bloc" with the internal sphincter usually through the perineal wound with a "pull through" technique, and then an additional laparotomy is not necessary. So this technique comes very close to the NOTES procedures.

Standardised surgical technique of the laparoscopic part of intersphincteric rectum resection

Pneumoperitoneum and port-positions

A pneumoperitoneum is facilitated in the right side of the umbilical ring with CO_2 gas, after patient-positioning, and desinfection of the abdominal wall, through the Veres needle with the "closed technique": after a 1 cm long incision, positioning of the Veres needle through the abdominal wall into the abdominal cavity. Through this needle, the abdomen is allowed to be insufflated to the pressure of 12 mmHg. The 11 mm blunt optic port is inserted through the Versa-step Veres-needle. In patients after previous abdominal operations, an open access of the first port is recommended.

After the initial diagnostic laparoscopy under continuous optical control, a 5 mm port is inserted 3 cm from the right superior iliac spine, and also a 5 mm port is inserted in the same line, between the umbilicus and this port. The third 5 mm port is inserted in the medioclavicular line, left from the umbilicus (Fig. 4).

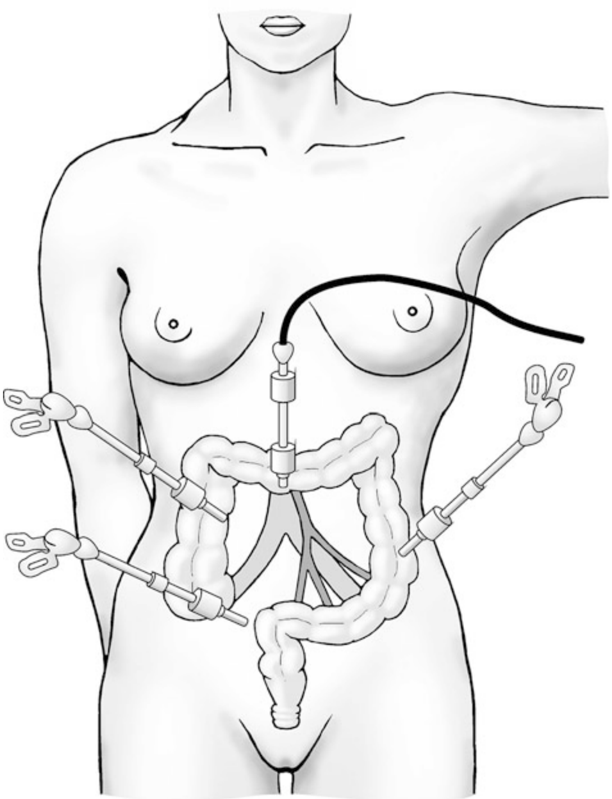


Fig. 4. Positioning of the ports

Beginning of the laparoscopic preparation

The beginning of the laparoscopic preparation in the abdominal cavity is a matter of controversy and dispute. Many authors prefer the preparation and early dissection of the inferior mesenteric artery and the visualisation of the autonomic nerves (N. Hypogastrici) on both sides.

We start with the identification of the left ureter, this is in our opinion one of the most important steps of the laparoscopic mobilisation of the left colon. This part of the preparation is an "insurance" for the safe preparation between the vascular-free embryologic fascias of the left colon, and: it gives us an excellent "navigation" to the left colonic flexure.

The laparoscopic procedure begins with a lateral to medial retroperitoneal dissection of the left mesocolon, with visualisation of the left ureter, first laterally, and later medially.

The preparations along the left ureter is begin from lateral side, with the opening of the Toldt's line. After the incision of this line the embryonal space is opened between the perirenal fatty tissue and the visceral fascia of the left colon. This space is our way to the left ureter. The descending colon is pulled medially using an atraumatic bowel clamp inserted from the right side via the port near the right iliac spine. With this simple method the visualisation and protection of the left ureter and gonadal vessels are easy (Fig. 5).

For the preparation along the ureter a monopolar electrocautery, a Ligasure™ or a Harmonic scalpel™ can be used. We prefer a Ligasure dissector for a precise dissection. The preparation of the left colon can be continued with the Ligasure™ until the caudal point of the splenocolic ligament. After this procedure the descending colon is pulled medially using an atraumatic bowel clamp in the right port by superior iliac spina.

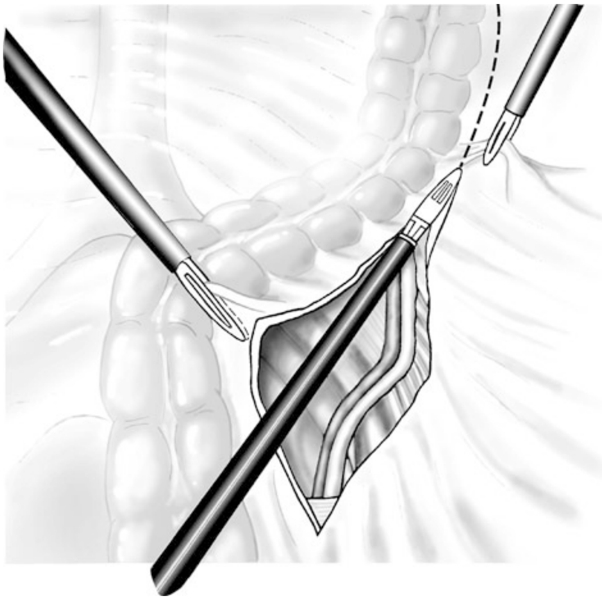


Fig. 5. Opening of the Toldt's line

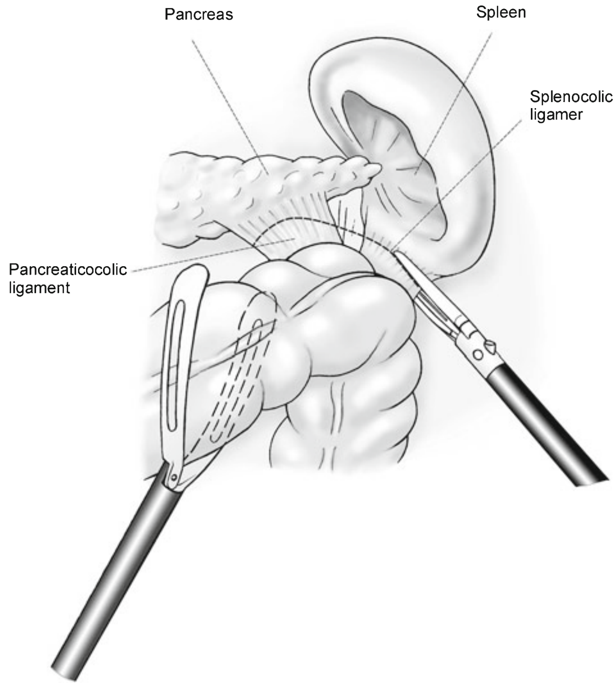


Fig. 6. Mobilisation of the splenic flexure 1

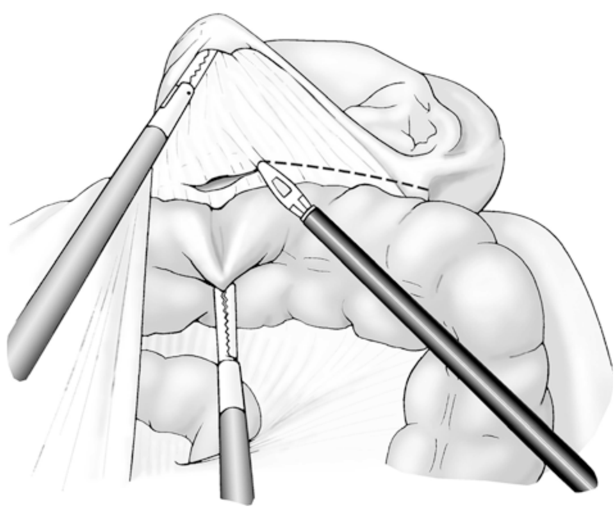


Fig. 7. Mobilisation of the splenic flexure 2

Should we always mobilise the splenic flexure in the surgery of the lower rectal cancer?

What is the aim of the mobilisation of the splenic flexure?

The mobilisation of the left colonic flexure as a standard technique in laparoscopic resection of the rectum is a matter of controversy in laparoscopic rectal surgery [6].

For many authors splenic flexure mobilisation is not required as a routine for a safe anterior low resection in patients with rectal cancer. Avoiding this procedure results in shorter operative times and does not increase postoperative morbidity, anastomotic leakage, or local recurrence. Mobilisation of the flexure does indeed carry a small risk of damage to the spleen but this is often a capsular tear from adhesions from the colon and seldom results in splenectomy.

In laparoscopic surgery of low rectal cancer one of the greatest technical challenges may be to make a **tension-free coloanal** anastomosis. A tension free left colon has – after the mobilisation of the splenic flexure – a greater chance for optimal positioning in the pelvic floor. A well vascularised, compliant segment of the left colon – with the mobilised splenic flexure – anastomized to the ano-rectal junction and under no tension has to be the goal in the intersphincteric resection.

After mobilisation of the left colon, the greater omentum is turned over the transverse colon, with a bowel clamp. The procedure progresses into the bursa omentalis, between the transverse colon and the stomach, throughout, dedicated assistants should provide the traction and counter-traction to open the correct planes. The surgeon may stand between the patient's legs and continue the dissection toward the splenic flexure, connecting this dissection with the lateral dissection, allowing the left flexure to be fully mobilised (Figs. 6, 7).

In case of a very long sigmoid the mobilisation of the splenic flexure is not necessary. We should make our decision dependent on the anatomic situation.

Division of the inferior mesenteric vessels

In more of the largest reports, there is no evidence that the high ligation of the inferior mesenteric artery confers an oncological advantage [7] analysed the data of 567 Dukes C' patients and reported no improvement in survival with proximal ligation. After analysis of 250 patients, 60% of whom had undergone inferior mesenteric artery ligation above the ascending left colic artery, there was no reduction in local recurrence or distal metastases [8].

The lymph nodes around of the inferior mesenteric artery are important and have a central role in the oncological radicality of the operation. The pedicle must be gently lifted with a bowel clamp to open up the correct embryologic plane precisely between the inferior mesenteric artery and the preaortal and preiliacal plane. This procedure is started with a bowel clamp, inserted through the right 5 mm port, in the line of the medioclavicular line. Dissection proceeds to the origin of the inferior mesenteric artery. The preparation around of the pedicle and the division of the inferior mesenteric vessels is performed – after the dissection of the left colon and splenic flexure – by a Ligasure™ dissector about 1–2 cm ventral from the abdominal aorta in order to spare the sympathetic nerve plexus, to be seen over the adventitia of the aorta. Arteries with a diameter >5 mm should be dissected with a vascular stapler (Fig. 8). The inferior mesenteric vein is identified and divided – also with a Ligasure dissector – above its last branch close to the pancreas.

The sigmoid mesenteric tissues are divided in the line between the pedicle and the lowest point of the descending colon, towards the planned line of resection (Fig. 9). The complete left colon can then be pulled into the pelvic floor. The distal end of the dissection and mobilisation of the left colon with the splenic flexure is then completed.

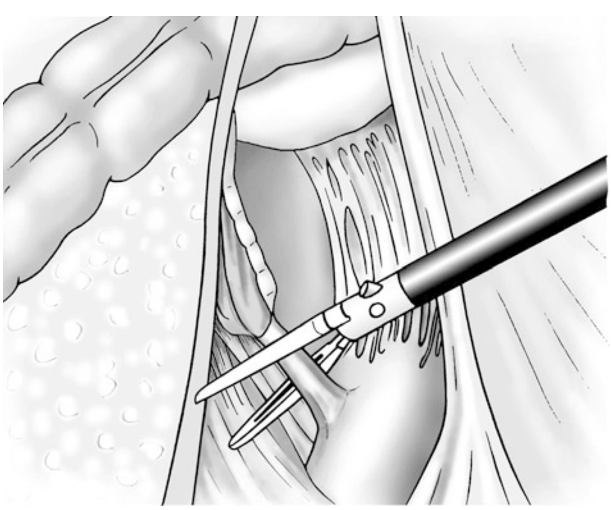


Fig. 8. AMI – dissection

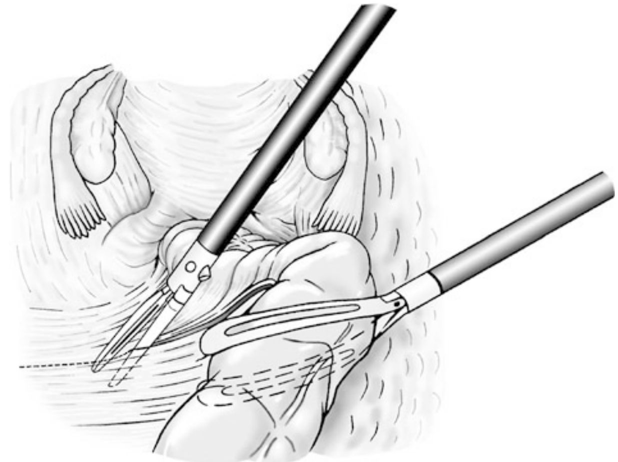


Fig. 9. Dissection line of the sigmoid mesenteric tissue

Laparoscopic TME

Routine excision of the intact mesorectum during the resection of cancers of the rectum has resulted in the lowest incidence of local recurrences ever reported [10]. Before starting pelvic dissection it is important to locate, at the level of the sacral promontory, the cleavage between the parietal layer ("presacral fascia") of the pelvic fascia and the visceral layer that underlines the mesorectum. This is an avascular space and by ventral traction we can demonstrate the shiny posterior surface of the mesorectum within the bifurcation of the hypogastric plexus at the superior part of the pelvic floor. We should begin with the ventral traction and with the incision from the left side. By preserving the left parietal layer, one avoids the risk of injuring the hypogastric nerves on both sides.

Lateral dissection

The peritoneum is then incised with Ligasure, step by step, along the left side of the rectum down to the retrovesical or retrovaginal reflection. The peritoneum can be incised along the left side of the rectum, beginning at the distal endpoint of the left colonic dissection lines. With some "help" of the pneumoperitoneum ("pneumodissection") the left lateral avascular plain between the left lateral pelvic fascia and the mesorectum can be opened. After completed incision on the left side of the pelvis the hypogastric nerve and the ureter should be followed

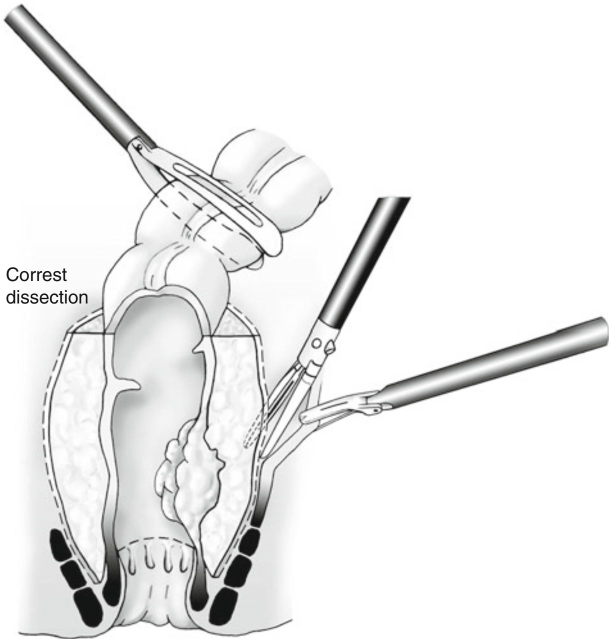


Fig. 10. TME – Lateral dissection

along its course. The same procedure is applies on the right side (Fig. 10).

Dorsal dissection

The dorsal dissection of the rectum is performed between the mesorectum and the parietal pelvic fascia in order to preserve the hypogastric nerves. The dissection continues down the presacral space in the avascular plane toward the pelvic floor: from both sides toward the endopelvic fascia and levator muscle (Fig. 11).

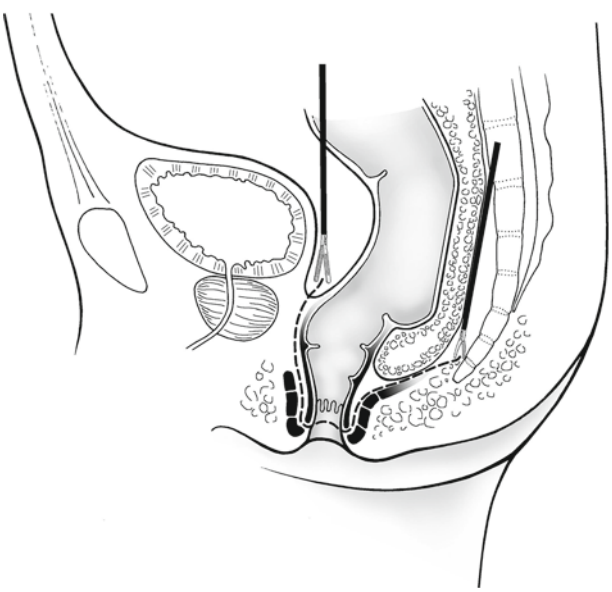


Fig. 11. TME – Dorsal and anterior dissection

Anterior dissection

Great care is taken to preserve the neurovascular bundle during the anterolateral dissection. The rectum is mobilized with scissors or with the Ligasure™ dissector, at the level of the seminal vesicles or rectovaginal septum on both sides: dorsal from the neurovascular bundle, in the Denonvillier's fascia (Figs. 12–14).

This maneuver facilitates an easier dissection along the anterior wall of the rectum, down to the anal canal. An

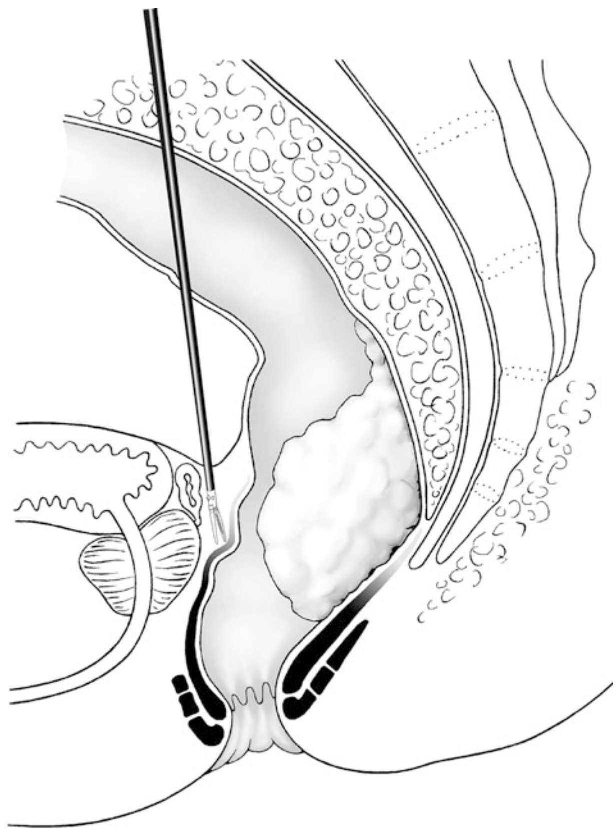


Fig. 12. TME – Anterior dissection

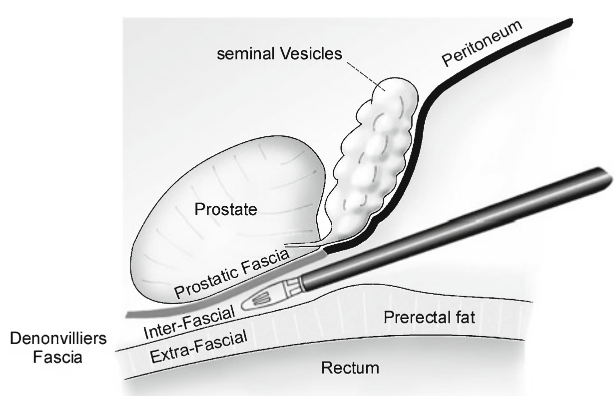


Fig. 13. TME – Anterior dissection

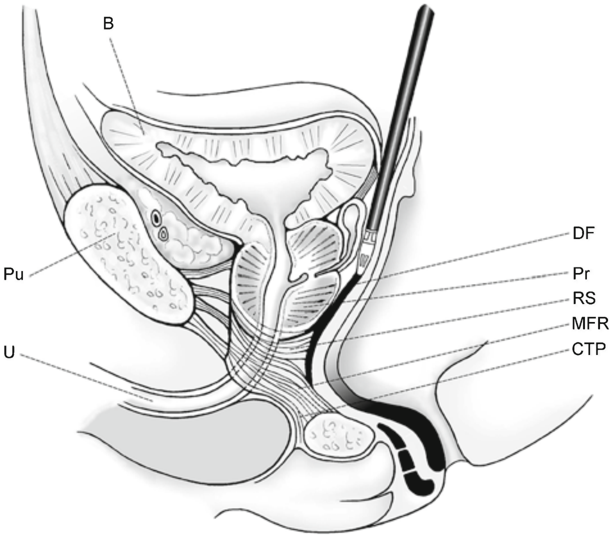


Fig. 14. TME – Anterior dissection

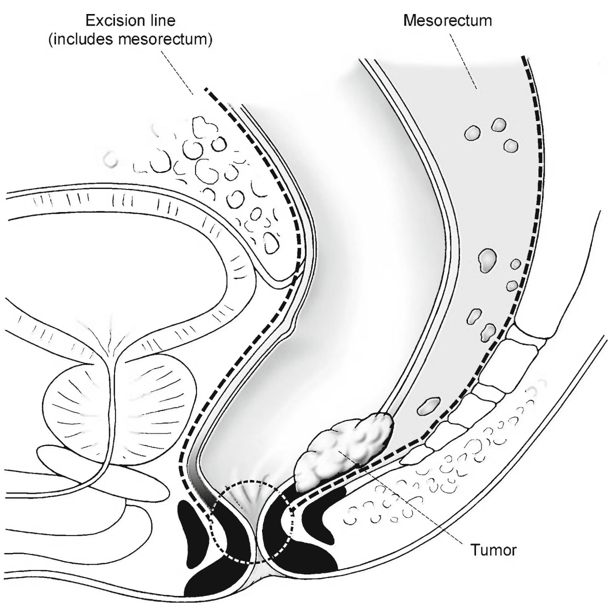


Fig. 15. TME – completed dorsal and anterior dissection

atraumatic bowel clamp is used to retract the prostate or vagina upward (via left 5 mm port). The antero-lateral dissection may then be continued, and is extended posteriorly to the Waldeyers's fascia. This is our practical surgical dissection plane (Fig. 15) [11].

End of the mesorectum

The mesorectum has a good, definite end: about one or two centimetres above the anorectal angle, the sling of muscle forming the anal hiatus of the pelvic diaphragm [12].

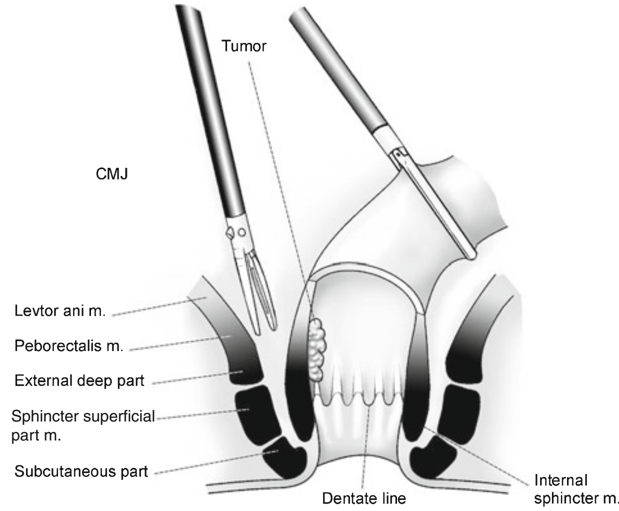


Fig. 16. Laparoscopic dissection into the intersphincteric space

This dissection can be very difficult, depending on the patient's obesity level, the diameter of the pelvic floor and the presence of bulky tumours.

Generally, one of the greatest difficulties in mesorectal excision may be the incongruence between the pelvic floor's diameter and the volume of the tumour masses. In this stage of the operation, more than in the previous stages, it is important to get adequate visualisation to complete the dissection.

The lowest point of the laparoscopic preparation is the upper part of the anal canal (Fig. 16).

With the new HD video technology, we broaden our horizons and gain a new view into the pelvic floor. But a significant limitation in performing laparoscopic TME for very low rectal cancer is the limitation of the endoscopic technology, the dissector and grasper or Ligasure™ cannot be passed low or precisely enough along an extremely curved and very narrow pelvic floor. We require long and flexible graspers, clamps, dissectors, and Ligasure™ dissectors.

During the aforementioned part of the operation, the "per anal team" began their preparation as soon as leg elevation was possible depending on the progress of the abdominal team.

Perineal part

The anus is dilated with a Lone Star™ retractor (Lone Star Medical Products, Stafford, TX). The first step is the infiltration of the intersphincteric groove with 0.5% Suprarenin solution. The anal canal is visualised, and the mucosa is incised with scissors, below the dentate line. The incision is circumferential and extends through the mucosa, the submucosa, and directly through the internal sphincter muscle: into the intersphincteric groove, and onto the external sphincter muscle. The dissection should start away from the tumour so that the proper plane can initially be identified, and the area affected by cancer can be approached at least.

The most difficult part of the dissection is the anterior circumference between the rectum and the prostate or vagina. In males, it is important not to proceed beyond the intersphincteric plane, as it is possible to damage the urethra. Again, it is better, if possible, to get the posterior and the lateral part of the dissection well started before moving to the anterior part. The dissection proceeds proximally, staying just on the external sphincter muscle. The critical issue during the dissection in this space is whether the external sphincter muscle is free of tumour or not [5]. If the intersphincteric plane and the external sphincter muscle are infiltrated with tumorous tissue, the attempt of sphincter preservation should be aborted. A minimal infiltration can be treated by segmental resection and immediate reconstruction of the external sphincter.

This plane can be followed well up into the pelvis, to a point just beneath the seminal vesicles or cervix uteri. This is the juncture at which a "rendezvous" with the laparoscopic team is appropriate; they should already be in waiting position with continous optical control of the lower pelvis.

Befor the rendezvous manoeuvre the intraabdominal gas pressure has to be lowered to 6 mmHg in other to avoid a sudden loss of vision for the abdominal team when a connection between the abdominal cavity and the perineum is facilitated.

The specimen will be removed through the perineal wound ("pull through") and the colon will be dissected with a linear-stapler (GIA™), from the perineal team. The coloanal anastomosis is constructed at the dentate line, or below according to the primary incision of the anoderm.

The anastomotic single sutures must be placed carefully, to include the anoderm and also the external sphincter muscle with the full intestinal wall. The resected specimen should be submitted to histopathological evaluation.

The final step of the operation is a protective ileostomy. This is closed after 6 weeks provided that an anastomotic fistula is excluded by a contrast enema examination.

Clinical and pathological data

There were forty nine patients enrolled in the period from October 2004 to December 2009, 28 males and 21 females, with the mean age of 61 years (range: 42–75 years) (Table 1). Forty-seven of the 49 patients were analyzed. Two patients were excluded from the follow up due to a postoperative necrosis of the neorectum.

Table 1: Characteristics of 49 cases (2004–2010)

Number of patients	49
Male	28
Female	21
Age range (yr)	61 (42–75)
Follow-up (median, month)	28 (12–48)
Tumor grading	
Well differentiated (G1)	27
Moderately differentiated (G2)	20
Poorly differentiated (G3)	2
CRM (Circumf. Res. Marg.) positiv	1 (Tumor infiltration into the prostate)

All patients had laparoscopic TME and complete resection of the internal sphincter after complete bowel preparation. All 49 patients had a defunctioning loop-ileostomy. Curative resection of malignant tissue with microscopically clear oncologic section margins was confirmed by postoperative pathologic diagnosis in 48 of the patients, one patient had a R1 resection. No deaths occurred during operation or in perioperative time.

There were 44 cases of adenocarcinoma (27 well differentiated, 20 moderately differentiated and two poorly differentiated), 3 villous adenomas with cancer tissue and 2 villous adenomas without cancer tissue. 13 patients had preoperative long term radio-chemotherapy.

For pathological stages, there were 12 cases at T1, 20 at T2, 13 at T3 and four cases (two after neoadjuvant radio-chemotherapy, two with villous adenoma) at Ty0 (Table 2). In these 49 patients, there were two cases with postoperative necrosis of the neorectums and two cases of postoperative anastomotic stenosis. Postoperatively, bowel frequency six months after operation ranged from one to six times per day. Only one patient had a positive CRM, despite partial resection of the prostate, with a late

Table 2: Pathologic results of 49 cases (2004–2010)

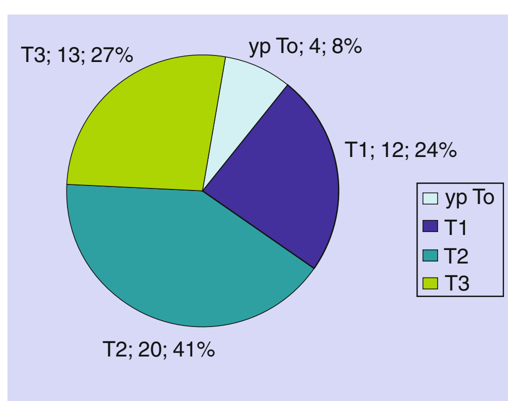


Table 3: Recurrence, survival of 49 cases (2004–2010)

Follow-up (median, month)	28 (12–48)
Local recurrence	0
Distant metastasis	1 (2%) (lung, 1 year postoperative)
Survival rate	98%
Disease-free survival rate	95.91% (47/49)

(1 year postoperatively) local recurrence and lung metastasis (Table 3).

Operation data, Complications

In both cases with neorectum necrosis, a relaparotomy with resection of the neorectum and a *permanent stoma was necessary. Median follow-up length was 28 months, without a local* recurrence. Our operation time ranged from 180 to 311 minutes, with a mean duration of 219 minutes.

In three patients' cases a conversion was necessary (bulky tumours in a small pelvis, and adhesions after a prior open surgery). A postoperative transfusion was not necessary (200 ml average blood loss) in any case.

- No deaths occurred during the operation or in perioperative time.
- During the follow-up period of 12 to 48 months, 100% of patients survived, and no patient developed pelvic or local recurrence.
- The incidence of postoperative ileus – oral from the loop ileostomy, such as strangulation – was 6.1% (three patients).
- Two patients (4.1%) developed clinical anastomotic leakage with fistula and later an anastomotic stricture.

Functional outcome

47 patients were evaluable. Forty-one patients (83.7%) have maintained capability to control solid or liquid stool and the capacity of flatus continence after the surgery.

Table 4: Functional results – postoperative continence

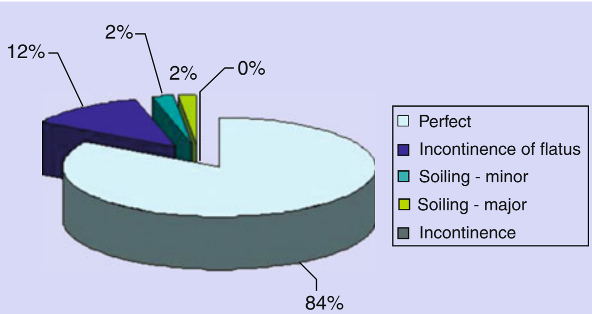
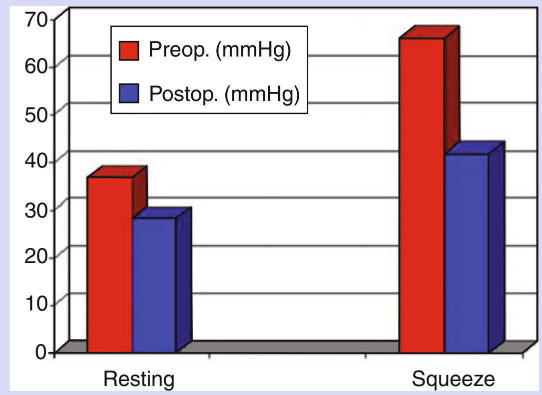


Table 5: Pre- and postoperative (6 month) manometry (mmHg)



Among these patients, 27 (55.1%) patients were able to control solid stool and occasionally lost continence of liquid stool. Only five patients have retained partial rectal function – with good continence of solid stool, but not liquid – after the operations, but the average times of defecation per day over the course of 36 months following the surgery were 3–5 times/day (Table 4). Anal manometry showed a decrease in pressure during the resting time after intersphincteric resection, and this change remained during the follow-up period (Table 5).

There was no case of erectile sexual disturbance among the 28 male patients, and the incidence of significant urinary voiding difficulty was 14% (4 patients).

Discussion

Today, the primary goals in the surgical treatment of rectal cancer are curative resection, when possible with complete or partial anal sphincter preservation as well as preservation of sexual and voiding function. A complete understanding of rectal and anal canal anatomy and of the adjacent pelvic organs is essential for colorectal surgeons who aim for optimal oncologic outcomes and safety in the surgical treatment of the very low rectal cancer. Over the course of the last ten years, one of the most crucial questions relative to surgery of this nature was solved: it is now clear that 5 cm distal margins are *not* needed to achieve good local control for rectal cancers.

The "gold standard" of rectal cancer surgery is the TME – Total Mesorectal Excision – defined and benchmarked by Heald [9]. He describes the three basic principles that one must understand and follow to perform a TME.

First, one must recognise that there is mobility between tissues of different embryologic origins. The rectum and its mesentery, encased by the fascia propria of the mesorectum are separate from those structures outside of this fascial envelope. The plane of dissection is just **outside** the fascia propria (the visceral endopelvic fascia) and just *inside* the parietal *endopelvic fascia.*

Second, the dissection must be performed sharply (no ripping, tearing or blunt dissection.), within a direct line of vision, with good illumination. The sharp dissection is generally performed either with scissors, or, more commonly, with the electrocautery.

Third, the plane must be gently opened by continuous traction and counter-traction, but not to the extent that the tissue tears or rips. This last factor is an integral surgical principle.

The surgical principle of the intersphincteric resection technique is based on the fact that the carcinoma expands primarily into the visceral structures. The anal canal is distally located, and there is an embryological plane between the visceral structures (internal sphincter muscle) and the surrounding skeletal muscles of the pelvic floor (external sphincter muscle). The aim of intersphincteric resection is to remove the internal sphincter muscles without damaging the skeletal (external sphincter) muscles [4].

The first step was a technique developed in 1977 for inflammatory bowel diseases [13]. The revolutionary publication from Schiessel et al. [4] marked the beginning of a worldwide surge in “sphincter saving” (although the correct classification may be “continence saving”) operation technique for low rectal tumors. In the last ten years many centres of rectal surgery published their experiences and results. It is a standardised and well reproduced technique, which has also very good functional results.

The first laparoscopic ISR was performed by Rullier in 2003 [14]. Data from small, non-randomised studies evaluating laparoscopic ISR suggest that this procedure is feasible for experienced surgeons, and a literature search identified numerous studies about laparoscopic intersphincteric resections: e.g. [15–18]. Intersphincteric resection (ISR) has been reported as a promising method for sphincter-preserving operations in selected patients with very low rectal cancer, in order to avoid a permanent stoma. Recently, several studies have reported largely successful short- and long-term results after ISR in patients with low rectal cancer [19].

On the basis of our long term experience with the technique of ISR and laparoscopic surgery we developed a new technique, by which two teams are working in parallel and in complement to one another. We have demonstrated that our new combined and modified ISR resection – which is based on the preparation along the anatomical structures – may be a shorter and also more effective technique than the “classical” ISR operation technique. Low conversion rate and the acceptable morbidity and mortality rate shows that the synchronous abdominoperineal laparoscopic intersphincteric approach itself was performed safely and feasibly. Our study analysed only a small number of laparoscopic surgeries retrospectively. A larger number of cases with very low rectal cancer operated by laparoscopic intersphincteric resection should be accumulated by a multicenter study. The safety and feasibility of this laparoscopic technique will then be confirmed or its limitations will be analysed.

Windows into the future

Future developments such as flexible instruments, 3D-visualisation and robotic instrumentation could further improve laparoscopic intersphincteric resection.

Over the last 20 years minimally invasive (laparoscopic) techniques have revolutionised visceral surgical practice. The second and third step of this revolution began with the single incision surgery, paralell to an enthusiastic development of many new instruments.

Another new way of the development of new instruments grows up from the roots of robotic surgery: articulated and semiautomatic manipulators and instruments might become a broad acceptance in laparoscopic colorectal surgery within the next years.

On the other side, it may seem that single incision laparoscopic technique (SILS) is just an expensive, complicated and time consuming form of laparoscopic surgery. First nonrandomised comparisons between conventional laparoscopic surgery and SILS are now available, and show that, in selected patients the technique is safe, and can be a real option.

The future is unknown, but the enthusiastic, revolutionary and experimental work on new instruments can be a good basis for the next generation of laparoscopic surgeons.

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Laparoscopic intersphincteric resection for ultra-low rectal cancer

Carlo Staudacher and Elena Orsenigo

Introduction

Local control of rectal cancer and patient survival has improved remarkably with advances in surgical techniques and adjuvant therapy. Because surgery is the only potentially curative treatment, progression in surgical management has played a central role. Historically, the earliest surgical approaches to rectal cancer were via the perineum. As surgical techniques and general anesthesia improved, other approaches such as a posterior approach were undertaken to improve access to the whole rectum. Consequently, abdominoperineal resection became the standard treatment until anterior resection was introduced for proximal rectal cancers. Abdominoperineal resection was the standard treatment for very low rectal cancer below 5 cm from the anal verge for many years. The first surgeon to report excising the rectum successfully was Jacques Lisfanc in 1826 [1]. The most important recent advance in rectal cancer surgery has been the advent of total mesorectal excision (TME), as proposed by Heald in 1982 [2]. He emphasized the importance of recognizing the “holy plane,” being one in which the surgeon’s dissection will encompass the malignancy and yet preserve autonomic neural function. Much recent surgical attention is now on the restoration of intestinal continuity. A combination of several approaches to the rectum was needed to avoid a permanent colostomy. By applying advanced surgical principles, surgeons can now excise most rectal cancers completely, often preserving the anal sphincter and leaving the patient with relatively normal bowel and pelvic function. Intersphincteric resection (ISR) is a technical development of extended low anterior resection for low rectal cancer which involves the mucosa of the upper anal canal. ISR does not have a long history. The technique was developed in the 1980s [3, 4] and accurately described by Schiessel et al. [5] who undertook the procedure to enable restorative resection and avoidance of a permanent stoma. ISR has expanded an indication of sphincter preservation for ultra-low rectal cancer and is now usually performed in combination with TME with abdominal anal approach. The technique of ISR modifies the concept of sphincter-saving resection in the treatment of rectal cancer. The decision between a conservative procedure and APR is not related to the distance between the tumor and the anal verge or the anal ring; it becomes solely related to the infiltration of the external sphincter. Cautious use of this operation has resulted in satisfactory defecatory function and oncological outcome [6]. The key steps of the operation described in the past included a laparotomy with mobilization of the left colon including the splenic flexure, autonomic nerve sparing rectal mobilization with total mesorectal excision down to the pelvic floor including division of Waldeyer’s fascia and anorectal mobilization within the puborectalis sling. When confronted with diseases requiring more invasive therapy, surgeons attempted to develop minimally invasive techniques that not only treated the disease process but also minimized patient morbidity. Minimally invasive surgery thus has a rich history spanning over many years. In the modern era, surgeons continued to develop minimally invasive techniques, particularly to treat colorectal diseases. Through minimally invasive techniques, surgeons could safely and effectively treat a larger patient population. The introduction of laparoscopic cholecystectomy in 1985 by Erich Muhe clearly illustrates the potential benefits of minimally invasive approaches to gastrointestinal diseases. Patients suffer less postoperative pain, develop fewer infections, earlier oral intake and are discharged sooner than after cholecystectomy performed through a standard Kocher incision. Laparoscopic cholecystectomy’s tremendous success, along with the flood of new technology into general surgery, stimulated surgeons to apply laparoscopic techniques to treat other gastrointestinal diseases. Laparoscopic colon resections are being performed with increasing frequency in the world, though the use of minimally invasive techniques in colorectal surgery has lagged behind its application in other surgical fields. Since the first laparoscopic colectomy was described in 1991 [7], a great deal of controversy has surrounded its use, particularly in the management of colorectal cancer. Several important new studies have demonstrated the benefits and safety of laparoscopic colorectal surgery, making it now the preferred approach in the surgical management of many colorectal diseases. After the publication of a report on the Clinical Outcomes of Surgical Therapy (COST) Study trial in 2004 [8] the laparoscopic surgery became an accepted practice in the management of colorectal cancer. With the publication of several multi-institutional, prospective randomized trials [8–10] it became clear that laparoscopic colectomy is equivalent to open colectomy in terms of oncologic safety for all stages of colon cancer. Nevertheless, there were and still are strong reservations regarding laparoscopic rectal cancer surgery with focus on inadequate oncologic resection and risk of tumor cell spillage because of traumatic manipulation of tumor, putting patients at risk of developing early recurrences. Also laparoscopic colorectal surgery entails a long and steep learning curve for the surgeon. Some surgeons were concerned that the minimally invasive technique would not be as good at removing all cancer cells from tissue around the tumour and that after a few years, the cancer would simply come back. This risk was thought to be highest for patients with rectal cancer. However, in a number of recent studies, laparoscopic and open excision of rectal cancer were found to be equivalent in achieving clear distal and radial margins, extent of resection, i.e. number of lymph nodes sampled, length of bowel and mesentery resected and bowel margins did not differ significantly between laparoscopic and open groups with satisfactory oncological control and functional outcomes [11]. These latest findings show that this is not the case and that in the hands of an experienced surgeon, the chance of rectal cancer recurring does not depend on the surgical method. Also, the overall survival rate of patients with rectal cancer is not affected by the type of surgery they have. There are some contraindications to the use of minimally invasive techniques in the treatment of rectal cancer, the most important of these being the presence of a T4 rectal tumor, not responder to neoajuvant treatment. When staging predicts invasion of adjacent pelvic organs (T4a disease) en bloc resection of involved organs is required to avoid tumour dissemination and positive resection margins. A multivisceral resection is defined as a surgical method resecting organs or structures adhering to the primary cancer en-bloc. In rectal cancer patients in which local tumor invasion to adjacent organs or structures is suspected a multivisceral resection must be performed. Despite being a radical strategy with high attendant risk and morbidity, multivisceral pelvic resection offers the possibility of long-term cure from locally advanced rectal carcinoma. Nevertheless, the presence of an involved margin after rectal cancer surgery is associated with local recurrence and poor survival. The use of neoadjuvant treatment to improve complete (R0) resection rates and maximize locoregional control and survival is firmly established in the management of locally advanced rectal cancer, but there is a quote of non-responders patients. Consequently, an en-bloc resection, a radical resection including adjacent organs and structures, is required. Whether the adhesion to adjacent organs was caused by direct invasion by the tumor or as a result of a simple inflammatory reaction could not be determined by using macroscopic examination only, but it could be determined based on pathohistological findings after surgery. Thus, many studies have reported that in cases when operative findings show suspected tumor infiltration, a radical resection, an en-bloc resection including adjacent organs and structures, achieved a good treatment outcome [12–15]. When invasion of tumors to adjacent organs is suspected, the separation of the adhered organs from the tumors has been reported to induce dissemination of tumor cells, thus elevating the local recurrence rate. As a result of these findings, rectal cancer patients requiring a technically difficult combination of resections involving intrapelvic organs must be excluded from the mini-invasive approach. However, laparoscopic approach can be applied in all the other cases. A literature search identified nineteen studies describing laparoscopic intersphincteric resection [16–35]. Laparoscopic rectal resection is considerably more difficult than colon resection, due to the narrow confines of the bony pelvis, and the need to identify retroperitoneal structures such as the nerves that control sexual and bladder function. Laparoscopic surgery has been reported to be one of the approaches for total mesorectal excision (TME) in rectal cancer surgery and, after then, laparoscopic intersphincteric resection has been proposed as a promising method for sphincter-preserving operation in selected patients with very low rectal cancer.

Indications, advantages, and disadvantages of laparoscopic intersphincteric resection

Information concerning the depth of tumour penetration through the rectal wall, lymph node involvement, and presence of distant metastatic disease is of crucial importance when planning a curative rectal cancer resection. Preoperative staging is used to determine the indication for neoadjuvant therapy as well as the indication for local excision versus radical cancer resection. In appropriate patients, minimally invasive procedures, such as local excision, TEM, and laparoscopic ISR allow for improved patient comfort, shorter hospital, and earlier return to preoperative activity level. Most patients are candidates for a laparoscopic approach. When the surgeon is experienced, even patients with a history of abdominal surgery are candidates. Though there are clear benefits, they have not been as compelling when compared to the clear advantages associated with other laparoscopic procedures. Even if long-term benefits are equivalent between open and laparoscopic techniques, the short-term benefits are real advantages for patients. In practical terms, the laparoscopic approach is associated with less pain, a faster recovery, earlier return of bowel function, a shorter hospital stay, possible immune benefits, and smaller scars, making it the preferred method for colorectal resection.

Exclusion criteria for laparoscopic intersphincteric resection

1. Presence of distant metastasis
2. Locally advanced disease with invasion into adjacent pelvic organs
3. Acute bowel obstruction or perforation from cancer
4. Severe medical illness.

All patients provide written informed consent. All patients are evaluated before operation by colonoscopy and a preoperative biopsy is routinely taken. The T number, the distance from the anal verge to the lowest edge of the tumor and the regional lymph node involvement are determined before operation by flexible endoscopic ultrasound and MR. CT abdomen is routinely done to rule out metastatic disease. CEA levels are routinely noted preoperatively. All patients receive mechanical bowel preparation the day before the operation. Systematic prophylactic antibiotics are given i.v. one hour before surgery. Pharmacologic venous thromboembolism prophylaxis (VTE) is administered to all rectal cancer patients for the duration of their hospitalization and extended up to 4 weeks post-operation. VTE prophylaxis is recommended for high-risk surgical patients. Urinary catheter is routinely used. No nasogastric tube is used. Neoadjuvant treatment is routinely offers to local advanced rectal cancer (all T stage with nodal involvement or node negative T3-T4 stage). The distance from the anal verge to the anastomosis is also measured by rigid proctoscopy. Sphincter function is assessed by measuring length of the pressure zone, maximum resting pressure, and maximum queeze pressure by anal manometry. Good postoperative pain control is a mandatory component of adequate postoperative care if accelerated recovery is aimed. Intraoperative and postoperative analgesia was provided by epidural analgesia (Fig. 1).

Fig. 1. Epidural analgesia. The skin is infiltrated with local anaesthetic such as lidocaine over the identified space. The insertion point is usually in the midline. The needle is inserted to the ligamentum flavum, is attached to a syringe in the peripheral end, and slowly advanced between two spinous processes. The loss of resistance to injection technique is used to identify the epidural space

How is laparoscopic intersphincteric resection done?

The technique of laparoscopic intersphincteric resection has a long learning curve because of the advanced laparoscopic skills it entails. Unlike other laparoscopic procedures, such as the Nissen fundoplication or cholecystectomy, rectal procedures involve dissection and mobilization of intra-abdominal organs in multiple quadrants. Scrub nurse plays key roles in the operating room (Fig. 2). An insufflator blows carbon

Fig. 2. Scrub nurse is extremely valuable member of the surgical team, providing support in the operating room

Fig. 3. Operating-room table

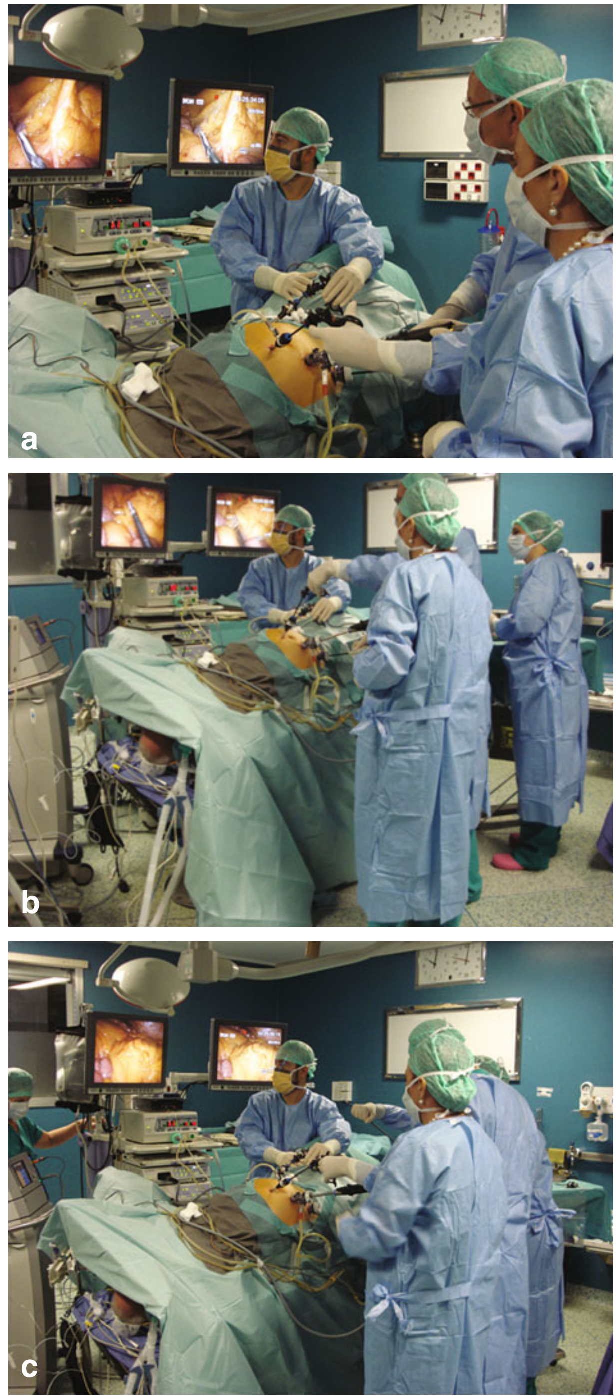

Fig. 4a–c. Surgical team

dioxide (CO_2) into the peritoneal cavity, creates a pneumoperitoneum. Tilting of the operating-room table in various positions during the operation uses gravity to allow intra-abdominal organs to fall away from the area of dissection, providing necessary exposure that would normally be achieved through the use of retractors (Fig. 3). Rectal resection requires laparoscopic ligation of large vessels, mobilization and removal of a long floppy segment of colon, and restoration of intestinal continuity. Laparoscopic intersphincteric resection is performed by a surgical team consisting of one surgeon and two assistants (Fig. 4). Patient is placed in head down Lloyd-Davies Trendelenburg position (Fig. 5) with the perineum slightly projecting from the end of the operating table, under general anesthesia with surgeon and camera assistant on patient's right side. Lloyd-Davies was born on January 13, 1905. He received his medical education at the Middlesex Hospital in London. In 1935, at the age of 30, he was appointed to the staff of St. Mark's Hospital. Lloyd-Davies was regarded as a slow and meticulous surgeon. He was also an original thinker and designer of instruments for colon and rectal surgery. His most well-recognized contribution was the development of specially designed leg supports as a means for providing access to the abdomen and to the perineum in the abdominoperineal resection. The lithotomy-Trendelenburg position become to be associated with his name. He described this position in a historical paper published in 1939 [36]. The aim has been to simplify operations on the pelvic portion of the bowel by placing the patient in such a position that a whole choice of procedures are available without moving or turning the patient once the operation has begun; for it to be possible to work either from the abdomen or the perineum, or alternatively, if there are two operators, for synchronous operating to take place. For laparoscopic intersphincteric resection 4 ports are routinely used. The camera port is inserted into the right midabdominal by open method. Trocars for low anterior resection are inserted into the right lower quadrant, the left midabdominal and at the umbilicus (Fig. 6). The

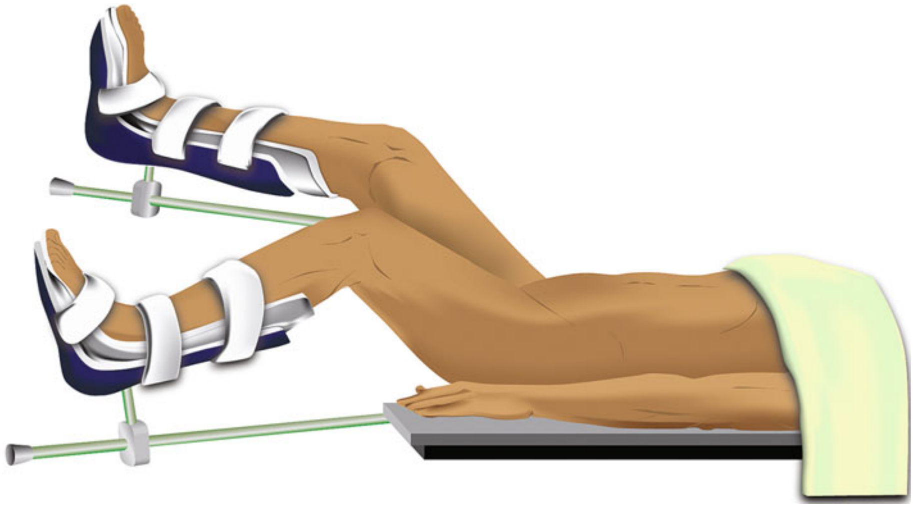

Fig. 5. Patient position

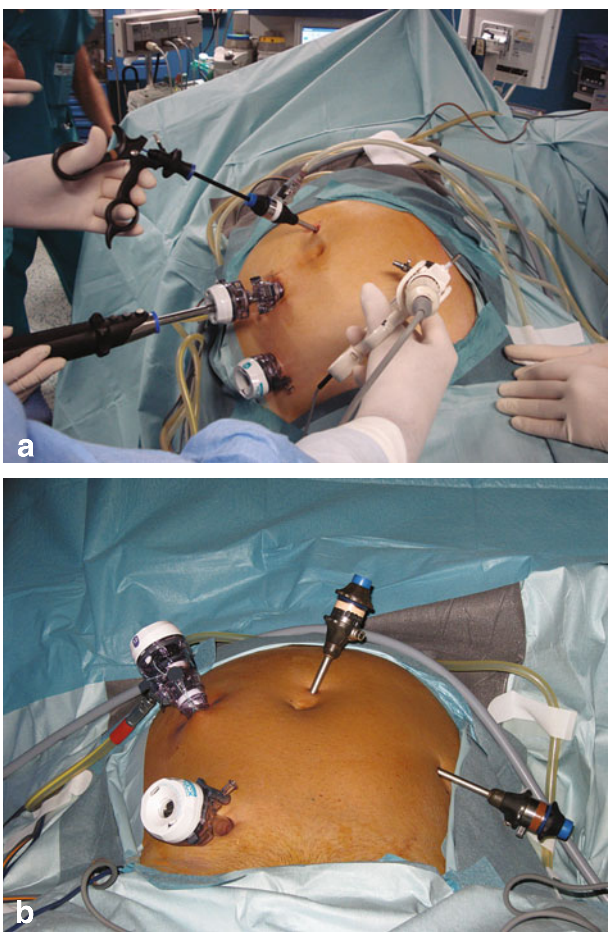

Fig. 6a, b. Trocars position

number of additional ports necessary is related to the complexity of the procedure. The surgical procedure is comprised of three stages. The first step of surgery is a laparoscopic trans-abdominal pelvic procedure. No deviation from basic principles of open oncologic rectal surgery is permitted and performed as follows: laparoscopic abdominal exploration, preliminary identification and transaction of inferior mesenteric artery (IMA) and inferior mesenteric vein (IMV) with linear stapler, mobilization of left hemicolon and splenic flexure, identification of ureters and hypogastric nerves bilaterally, rectal mobilization with TME. The IMA is taken 1–2 cm anterior to the aorta and the vein is divided close to the pancreas. During mobilization of the mesorectum care must be taken to avoid any damage to the underlying hypogastric nerve plexus (Fig. 7). Dissection is continued ventrally in front of the Denonvilliers fascia. Colonic mobilization, including release of the splenic flexure is performed by using an harmonic scalpel. The

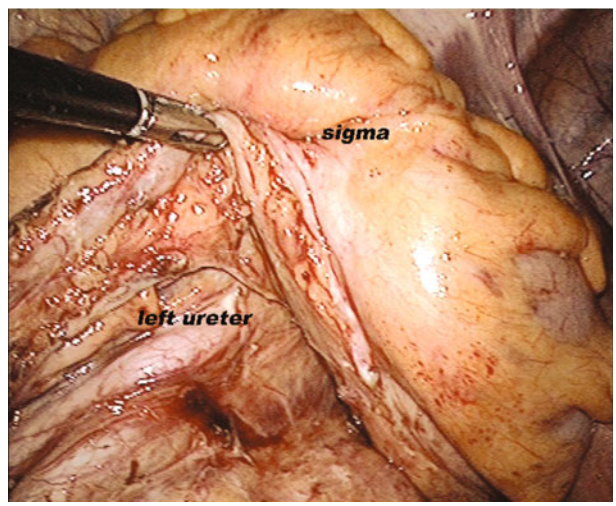

Fig. 7. Laparoscopic left colon mobilization

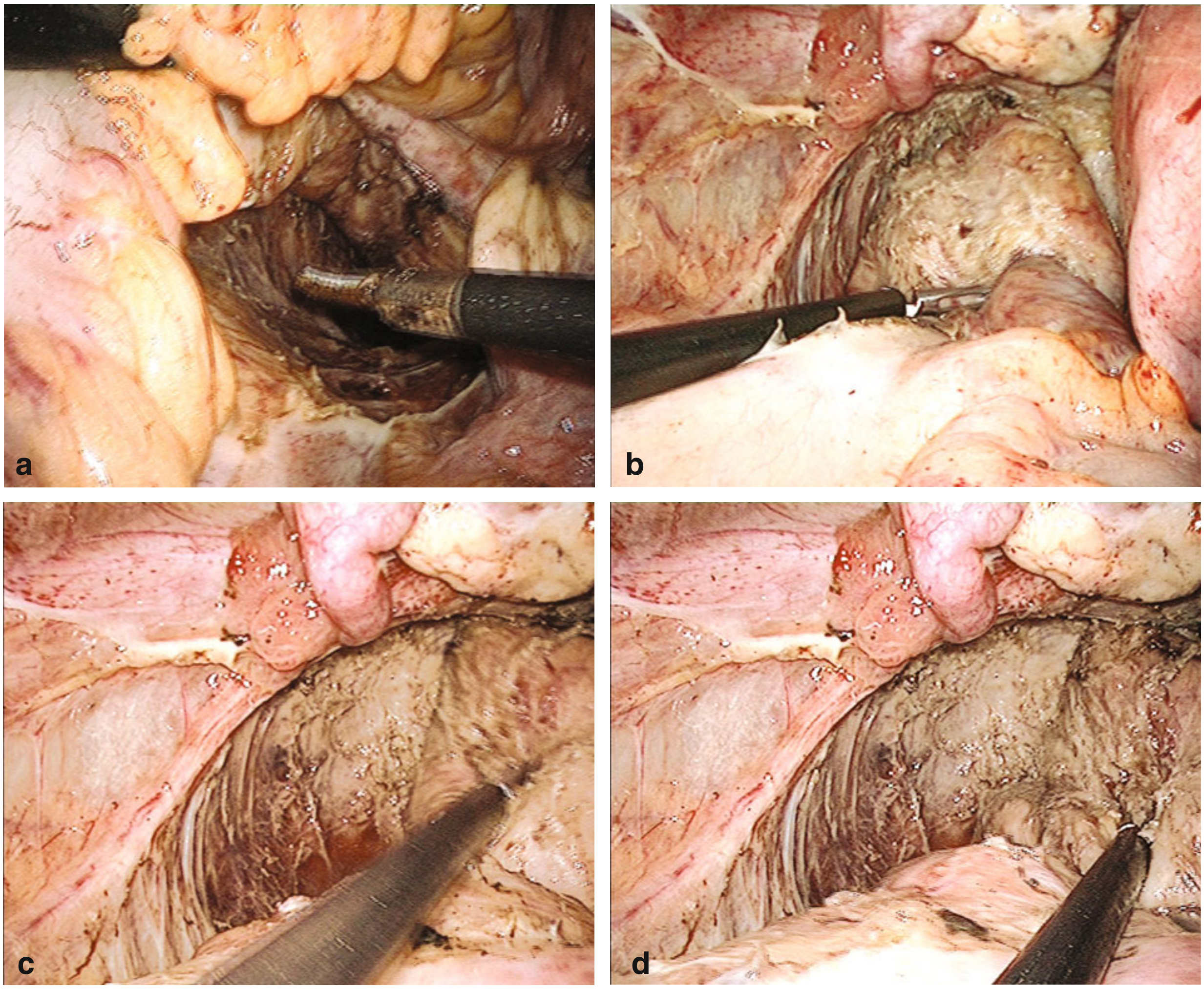

Fig. 8. Laparoscopic TME; (**a**) The Holy plane; (**b**) The anterior plane of rectum behind vagina; (**c**, **d**) dissection of lateral ligaments of rectum

left colon and splenic flexure are mobilized in their entirety, if necessary, to ensure that the colon reaches the anus without tension. Total mesorectal excision is performed with complete preservation of the autonomic nervous system (Fig. 8). On both sides of the rectum, the lateral second stage of surgery is the anal part of the operation. The application of a self-holding retractor (Lone Star Retractors, Lone Star Medical Products Inc., Houston, TX) positioned into the anal canal guarantees a comfortable access to this region (Fig. 9). After then, a circular incision of the anoderm is performed and the internal sphincter separated from the external sphincter and puborectalis muscles. Transanal division of the internal anal sphincter connects with pelvic dissection, allowing adequate distal margin. ISR started at the dentate line to remove the upper half of the internal sphincter for tumors 3 to 4.5 cm from the anal verge (partial or high ISR); it started below the dentate line, removing the whole of the internal sphincter for tumors below 3 cm from the anal verge (total or low ISR). After circular dissection of the tumour-bearing rectum, the specimen is delivered per anally (Fig. 10). After pull through of the descending colon the coloanal anastomosis is performed between the colon, the external sphincter, and the anoderm (Fig. 11). Finally, a pelvic drain is placed laparoscopically, and a protective stoma (transverse ileostomy or colostomy) is created by using a port site (Fig. 12). The use of loop ileostomy or loop transverse colostomy represents an important issue in colorectal surgery. The creation of an intestinal stoma (usually ileostomy or colostomy) brings a wide range of physical and psychological challenges. Physical complications directly related to a stoma have been reported widely in the medical literature and are often exacerbated by a suboptimal stoma (for example difficulty securing an appliance, leakage, and change in body image associated with a parastomal hernia). Furthermore, problems dealt with by stoma therapists

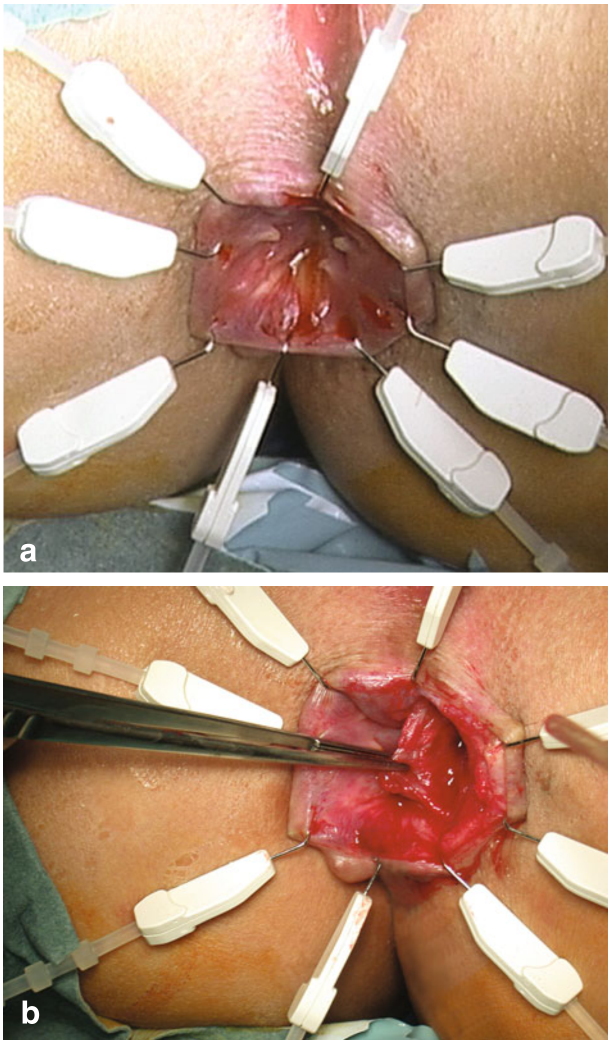

Fig. 9a, b. Perineal step of surgery

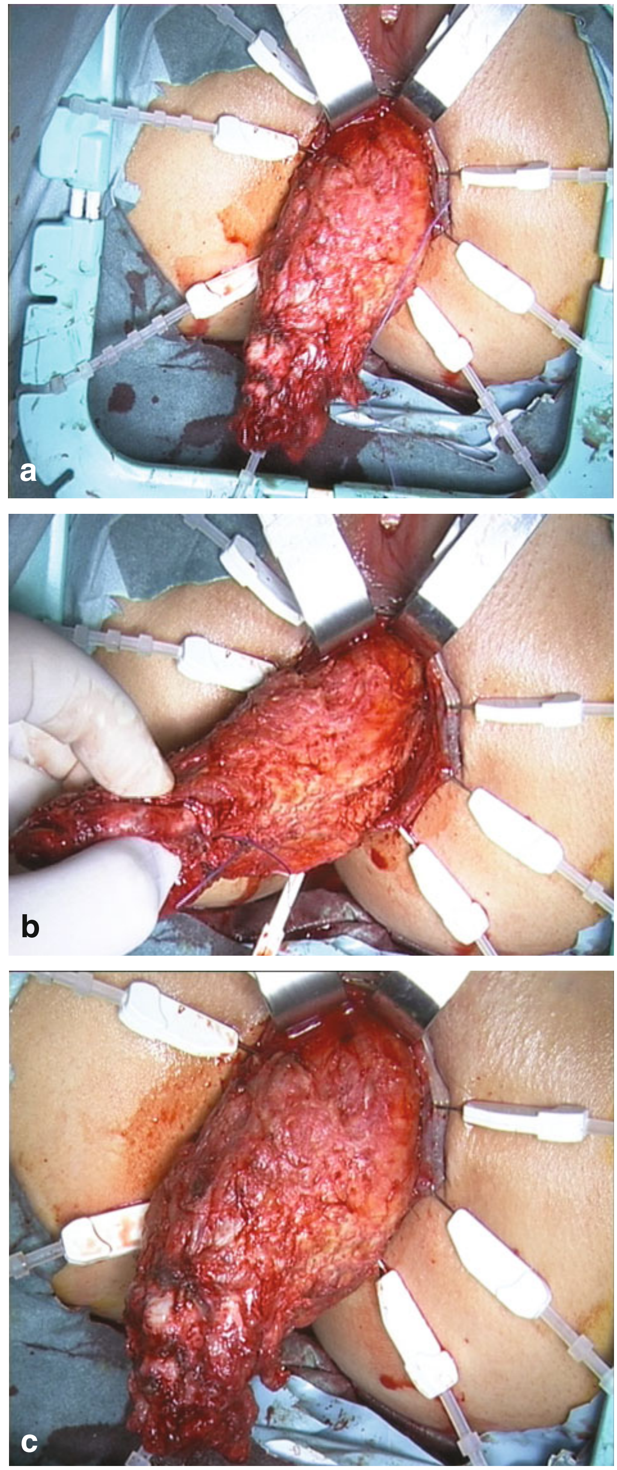

Fig. 10a–c. The specimen is delivered per anally

do not always reach the surgeon's attention, and reported complications based on medical records may underestimate their frequency. The overall major complication rates reported are 21–60 per cent [37–42]. The best available evidence for decompression of colorectal anastomosis, either use of loop ileostomy or loop colostomy, was not be clarified from the review of the Cochrane database [43], but ileostomy seems better than colostomy. Surgery to reverse a temporary colostomy or ileostomy (reconnection of the bowel) is a relatively minor procedure. Deciding when to do the reversal depends on a number of factors including how well the patient has healed after their initial surgery and how fully they have recovered from other treatments like chemotherapy or radiotherapy. Sometimes reversals can be done after a couple of weeks while in other cases it takes much longer (Figs. 13, 14).

Discussion

Ambroise Paré, a 16th century French surgeon, stated that there were to perform surgery: "To eliminate that which is superfluous, restore that which has been dislocated, sepa-

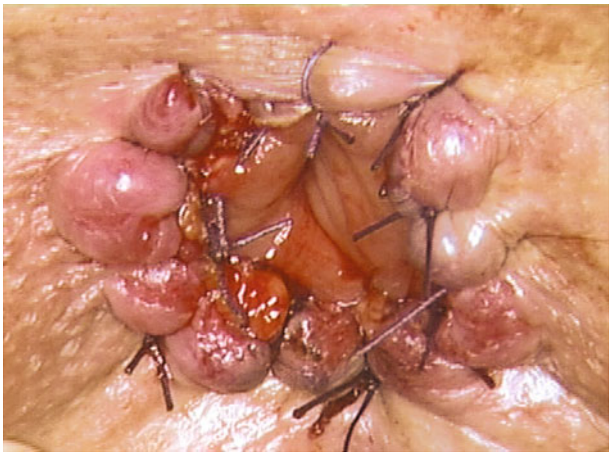

Fig. 11. Coloanal anastomosis between the colon, the external sphincter, and the anoderm

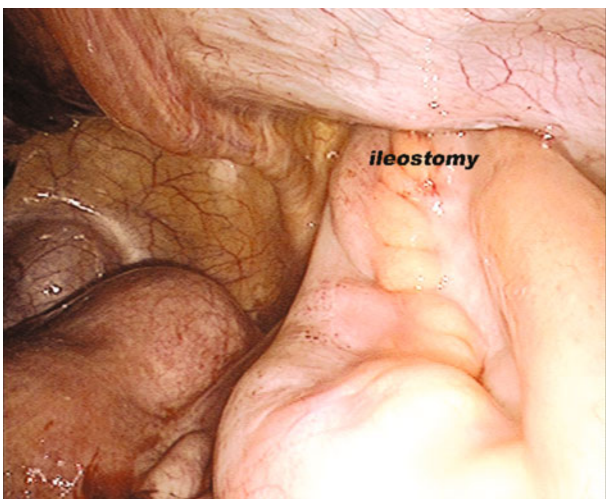

Fig. 12. Diverting ileostomy

Fig. 13. Control after surgery (1 month later)

Fig. 14. Result after ileostomy reversion

rate that which has been united, join that which has been divided and repair the defects of nature". Since humans first learned to make and handle tools, they have employed their talents to develop surgical techniques, each time more sophisticated than the last. In general, the surgeon has been considered the technician while the physician (more historically related to the priest and shaman) was the true healer. Following improvement in surgical skills and cancer therapy (chemotherapy and radiation therapy), the general consensus for rectal cancer operations has changed dramatically in the past decade. Sphincter-saving resection and the restoration of bowel continuity, is one of the main objectives of surgical treatment of rectal cancer. Methods of sphincter preservation were developed more than a century ago. Combining these techniques with adequate anterior resection has permitted the resurrection of sphincter-saving procedures that are currently being applied in the therapy of cancer at every level of the rectum. The surgical management of rectal cancers depends on a number of factors, including stage, tumor size, location within the rectum, depth of invasion into the wall of the rectum, and involvement of the sphincter complex. Select patients with small, superficial tumors with no evidence of spread to the lymph nodes may be candidates for limited surgery via a local excision. In cases of early rectal cancer, the transanal endoscopic microsurgery (TEM) procedure allows surgeons to treat lesions larger or higher in the rectum than ever before, rather than having to perform major abdominal surgery to remove all or part of the rectum. However, the majority of patients will require more extensive procedures such as low anterior resection or abdominoperineal resection for management of their rectal cancer. Current trends also suggest that the abdominoperineal resection is being used less frequently in the treatment of most rectal cancers and is being replaced with sphincter-preserving techniques that afford excellent functional results. It has become practical that fecal continence function can be preserved in the patients with lower rectal cancer. According to the tumor progression, the patients with a very low location of cancer are considered for radical resection of tumor even with only 1–2 cm between the distal margin of the tumor and the dentate line. Recently, ISR of rectal tumor combined with coloanal anastomosis has been used in patients with rectal cancers located less than 5 cm from the anal verge. The technique of ISR of tumors combined with coloanal anastomosis has been used to avoid permanent colostomy for patients with a rectal cancer located <5 cm from the anal verge. The surgical technique of ISR has been proposed to offer sphincter preservation in patients with very low rectal carcinoma. The goal of ISR is to divide the rectum transanally and to remove part or the whole of the internal anal sphincter, to obtain adequate distal margin and restore bowel continuity [35]. Because of laparoscopic surgery has been shown to have equivalent outcomes compared to open surgery for cancer of the colon, this technology is currently applied for the surgical treatment of rectal cancer. The restricted vision, the difficulty in handling of the instruments (new hand-eye coordination skills are needed), the lack of tactile perception and the limited working area are factors which add to the technical complexity of the laparoscopic approach. For these reasons, minimally invasive surgery has emerged as a highly competitive new sub-specialty within various fields of surgery. The benefits of laparoscopic surgery include improved cosmesis (preservation of appearance) from smaller incisions, decreased postoperative pain, shorter length of hospital stay, and earlier return to normal activity. However, laparoscopic surgery is also associated with longer operative times. While laparoscopic rectal resections are not the current standard of care, there are some experienced surgeons who are able to perform this procedure with excellent outcomes, but we also keep in mind that the goal of any cancer surgery is to successfully remove the cancer. An advanced laparoscopic procedure plays an especially important role in rectal cancer treatment. The result for most patients is a shorter hospital stay, a faster, less painful recovery, and preservation of normal bowel, bladder and sexual function. Laparoscopic surgery has been used in the treatment of intestinal disorders for close to 20 years, but its benefits have only recently begun to be extended to people with rectal cancer. Rectal surgery is inherently more challenging than colon surgery. For one, the pelvic cavity of the body where the rectum lies, is a narrow space, making rectal tumors difficult to access. Surgical success depends not only on the complete removal of the cancerous tumor and repair of the rectum, but also on restoring continence. For these reasons, rectal cancer has been a difficult arena to apply advances in minimally invasive surgery. It is only appropriate to perform laparoscopic proctectomy for curable cancer in an environment where the outcomes can be meaningfully evaluated until laparoscopic approaches have been shown to be as efficacious as open approaches. The ASCRS and SAGES encourage the development of properly designed studies to evaluate the safety, efficacy, and benefits of this approach. The ASCRS and SAGES consider laparoscopic proctectomy to be within the expertise of trained surgeons who focus on the treatment of rectal cancer. Development of this expertise should include observation of procedures, laboratory experience and graduated clinical responsibility as mentioned in published guidelines [44, 45]. Historically, the three major and decisive strides that have been made in the last two decades in the treatment of rectal cancer were the establishment of multimodality therapy, the introduction of total mesorectum excision, and the application of laparoscopy. Potential benefits in terms of improved cosmesis, reduced postoperative pain, early return of bowel active functional recovery and shortened hospital stay are proven benefits of laparoscopic colorectal surgery. Comorbidity does not appear to be a major obstacle for laparoscopic technique. And even elderly patients with comorbidities may be benefited with reduced postoperative morbidity. With magnified view and improved visualization of deep pelvic structures under laparoscope, laparoscopic rectal cancer excision should yield functional outcomes at least comparable. Laparoscopic resection for rectal malignancy might be the next step in the evolution of modern rectal cancer surgery. Moreover, single-incision laparoscopic surgery (SILS) is one of the most recent developments in laparoscopic surgery. Having proven its effectiveness in cholecystectomy and appendectomy, the feasibility of SILS in more advanced surgery, such as low anterior resection, is now a point of discussion and probably could be the evolution of the minimally invasive approach to rectal cancer.

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A concept of sphincter salvage in low rectal cancer

Eric Rullier, Quentin Denost, and Christophe Laurent

Introduction

Standard surgery in low rectal cancer is moving to more conservative surgery, due to development of new techniques, new concepts and specialization. The purpose of this article is to discuss the limits of the abdominoperineal resection (APR) procedure and the potential advantages of ultra low conservative surgery. A new surgical classification of low rectal cancer is also presented with the objective to standardize surgical management of low rectal cancer. The surgical technique of intersphincteric resection (ISR) is described, included the laparoscopic approach. Finally, personal results, in term of oncologic and functional outcome, as well as difficult cases are reported.

Limits of the abdominoperineal resection procedure

In 2011, APR is still the standard of care in surgical treatment of low rectal cancer, i.e. for tumours located below 5 cm from the anal verge. The first reason is historical, APR has been the first efficient procedure to treat rectal cancer [1] and therefore with which any kind of new procedure must be compared. The second reason is the oncologic concept of wide (extended) excision to cure cancer, imposing to remove the anal sphincter in patients with a rectal tumour. Surgical experience and better knowledge of distal spread of the disease permitted to propose sphincter preservation in high and mid rectal cancer, and more recently in some low rectal cancers [2]. Actually, most of the surgeons accept conservative surgery for tumours more than 2 cm from the anal sphincter, whereas most of the tumours less than 1 cm receive APR. Depending of the experience of the surgeon and specialization of the hospital, the rate of APR in rectal cancer surgery varies from 8% to 53% in England [3].

Before the technique of TME, APR was considered as the optimal procedure to treat low rectal cancer, whereas sphincter-saving resection (SSR) was suspected to increase the risk of local recurrence [4]. Since the introduction of the technique of TME, new data suggest the opposite [5]. Compared to SSR, APR is associated with a higher risk of intra-operative perforation and positive circumferential resection margin [6], which may compromise both local control and survival [5, 7]. The risk of dying was increased by 30% in Norway among patients with low rectal cancer who underwent APR compared with those having an anterior resection [7]. The reasons of the worse prognosis of APR patients are due to the fact that APR is not a well standardized procedure. The technical limit is the non anatomical perineal dissection, managed through the ischiorectal fat and the pelvic floor muscles without anatomical landmarks. The surgical limit is the non adapted concept, where most of the surgeons decide to perform SSR or APR after a full mobilization of the rectum, checking the distance between the tumour and the anal ring at the end of the dissection. These technical and surgical mistakes explain the “cone effect” of both perineal and pelvic dissections and therefore the unacceptable high rate of perforation and positive circumferential margin, which are located preferentially at the anorectal junction [5]. The inadequate surgical resection of the conventional APR has been underlined in Europe and a modern (called extralevator or cylindrical) APR has been proposed to improve oncologic results [8, 9]. The disadvantage of the extralevator APR is the difficulty to close the perineum.

Another disadvantage of the APR procedure is the higher rate of pelvic sepsis, as compared to anterior resection. Indeed, pelvic sepsis is associated with a higher risk of local and distant recurrence [10, 11]. This is due to inflammation response to chronic sepsis which enhances the tumour and metastatic spread via released cytokines [12]. Thus, the association between the opening of the pelvic floor and perineal tissues, potential chronic inflammation and a non optimal surgery (rectal perforation, cone effect) participates to the worse prognosis of APR.

By contrast, sphincter preservation presents several advantages [13]. The first is the three fold lower risk of intraoperative rectal perforation and positive circumferential margin than APR. As previously discussed, this is because TME with sphincter preservation is a more anatomical and standardized surgical procedure than APR. The second advantage is the better genital function observed after low anterior resection than after APR: 72–90% *vs*. 63–75% [14]. This is due to the lower risk of damaging the pelvic branches of the pelvic autonomic nerve, which are exposed during the perineal phase of an APR. The third advantage of conservative surgery is preservation of the body image that may increase quality of life. So, the oncologic and functional advantages of conservative surgery, as compared to APR, lead us to consider sphincter preservation, not as an option, but as a new gold standard in low rectal cancer.

Sphincter preservation: Evolution of the concept and new rules

The conventional concept for sphincter-saving resection is related to the distance between the tumour and the anal sphincter. A better knowledge of rectal cancer disease allows decreasing the distal surgical margin from 5 cm to 2 cm [15] and more recently to 1 cm [16, 17]. The surgical guidelines therefore recommend sphincter preservation in patients with a tumour more than 1 cm from the anal ring and APR for tumors less than 1 cm [18, 19].

The technique of intersphincteric resection (ISR) has been developed to push lower the conservative approach in low rectal cancer [20]. The goal is to divide the rectum transanally and to remove part or the whole of the internal anal sphincter, in order to obtain adequate distal margin and preserve the natural function of defecation. ISR is used mainly in Europe [21–24] and more recently in Asia [25, 26]. This technique modified the concept of sphincter preservation, because it permits theoretically to avoid APR in all rectal cancers due to possibility to obtain safe distal margin in all cases [27]. Furthermore, it is now admitted that circumferential resection margin is associated with local recurrence, with more evidence than distal resection margin [28, 29]. So, the conventional concept of the distal rule for sphincter-saving resection is replaced by the concept of the circumferential rule. The main limit for sphincter preservation is not the longitudinal distance between the tumour and the anal sphincter, but the circumferential distance between the tumour and the skeletal muscles of the pelvic floor. This new concept transforms a 1 cm discussion to a 1 mm one [30].

Series of intersphincteric resection confirm the safety of the procedure with 1.6% mortality, 10% of anastomotic leak, 9% of local recurrence and 81% of 5-year survival in a pooled analysis of 612 patients treated in 13 units by ISR for T2T3 low rectal cancer [31].

Bordeaux' surgical strategy for low rectal cancer

Neoadjuvant radiochemotherapy for rectal cancer [32] and the technique of ISR [23] are used at Saint-Andre Hospital, University of Bordeaux, since more than 20 years. Surgical management of low rectal cancer, including neoadjuvant therapy and ISR, is composed by the three following steps:

1. Classification of low rectal cancer in 4 types
2. Standardisation of surgery in 4 operations
3. Anticipation of surgery before and decision after neoadjuvant treatment

The **Surgical Classification** of low rectal cancer separates patients with rectal cancer below 6 cm from the anal verge in four groups according to the location of the tumour from the anal sphincter (surgical anal canal) (Fig. 1):

– Type I = Supra anal tumours: lesions located > 1 cm from the anal ring (top of the anal canal) or > 2 cm from the dentate line
– Type II = Juxta anal tumours: lesions located ≤ 1 cm from the anal ring or ≤ 2 cm from the dentate line
– Type III = Intra anal tumours: lesions with infiltration of the internal anal sphincter
– Type IV = Trans anal tumours: lesions with infiltration of the external anal sphincter or levator ani muscles

Standardization of surgery defines four surgical procedures, each dedicated to the four types of low rectal cancer (Fig. 1):

– Type I: Coloanal anastomosis (CAA), the internal sphincter is preserved
– Type II: Partial intersphincteric resection (pISR)
– Type III: Total intersphincteric resection (tISR)
– Type IV: Abdominoperineal excision (APR)

Classification of low rectal cancer is part of the initial staging of the tumour and is performed by consensus including digital examination by the surgeon, endorectal ultrasound and magnetic resonance imaging. It must be performed before neoadjuvant treatment. Rectal palpa-

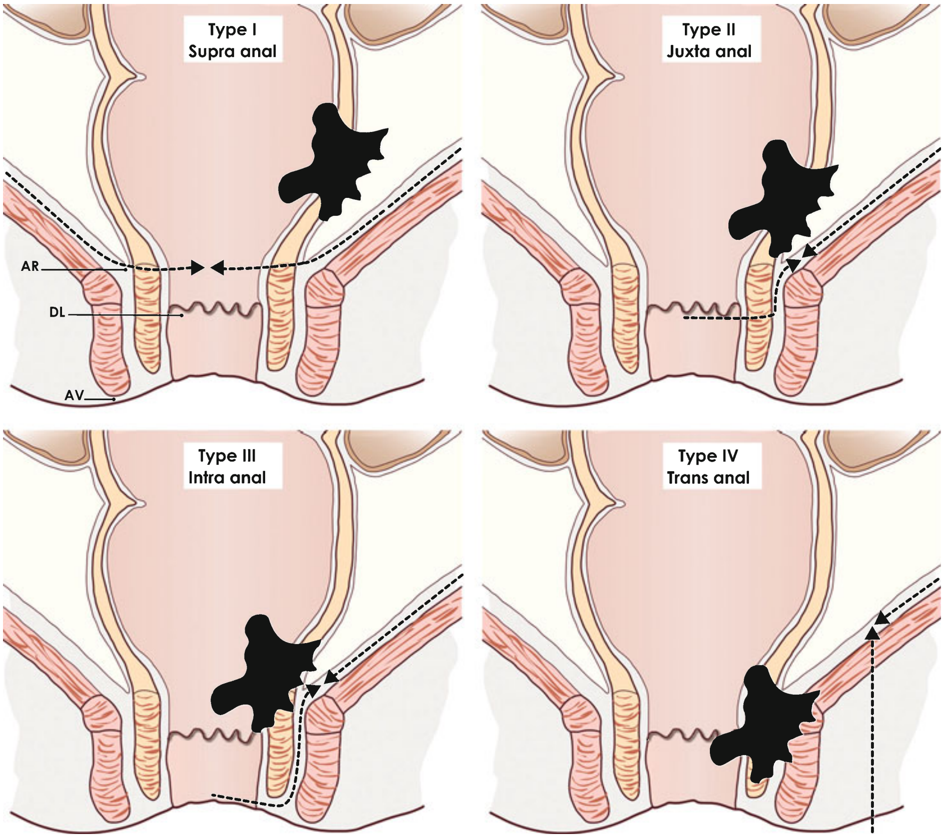

Fig. 1. Surgical classification of low rectal cancer. Type I are treated by conventional coloanal anstomosis, type II by partial ISR, type III by total ISR and type IV by APR. *AR* anal ring; *DL* dentate line; *AV* anal verge

tion with voluntary anal contraction permits to check the exact distance between the tumour and the anal canal. Examination under anesthesia is sometimes necessary, especially when the anal canal is involved or in case of fixed tumours. Rigid rectoscopy informs on tumour location and on distance between the tumour and the dentate line. Endorectal ultrasound and magnetic resonance imaging are necessary for tumour staging and to confirm clinical examination, in term on relation and distance between the tumour and the anal sphincter. Preservation of the intersphincteric plane at magnetic resonance imaging is the key point to differentiate types I, II and III low rectal cancers suitable for conservative surgery, from type IV treated by APR.

By using such classification, decisions for conservative surgery and subsequently type of conservative procedure are made (at least suggested) initially. In the past, due to the 2-cm distal rules, ISR was also proposed to some type I low rectal tumours. Since several years, it is proposed only for tumours type II or III, i.e. less than 1 cm from the anal sphincter. Early rectal tumors (T1T2) are treated by surgery alone, whereas advanced tumors (T3) and those with infiltration of the internal anal sphincter must be treated by preoperative radiochemotherapy. Such treatment reduces the tumor volume and induces downstaging that increases the circumferential resection margin [32]. One month after radiochemotherapy, a new MRI is performed to assess the tumour response. A good response increases the chance of R0 resection and therefore confirms the initial surgical strategy. A bad response (less than 10% in our experience) may modify the initial surgical strategy. The objective is to obtain a radiological CRM > 1 mm to the levator ani muscles and the external anal sphincter in order to propose conservative surgery. Surgery is performed two months after irradiation to optimize dowstaging.

In practice, low rectal cancers are managed as following:

– T2 supra and juxta anal tumours are treated by conservative surgery alone
– T2 intra anal tumours are treated by radiochemotherapy and conservative surgery
– Any T3 T4 low rectal tumours are treated by radiochemotherapy, and conservative surgery if 1 mm CRM and free intersphincteric plane at MRI one month after neoadjuvant treatment

Surgical technique of ISR

The principle of the technique is based on the facts that rectal tumors expand into the visceral structures, i.e. the rectum and distally the internal anal canal, and that there is an embryonic plane of fusion between the visceral structures and the surrounding somatic skeletal muscles of the pelvic floor. The aim is to remove the viscus without damaging the skeletal muscles.

Abdominal step

Surgery is performed six to eight weeks after radiotherapy. The technique of ISR combines the abdominal and the perineal approaches. The abdominal dissection is carried out first through a midline incision. A high ligation of the inferior mesenteric artery is performed together with a full mobilisation of the left colon, including splenic flexure, to facilitate a tension-free low anastomosis. Total mesorectal excision with preservation of the autonomic pelvic nerves is then achieved as low as possible to facilitate the perineal step. Anteriorly the dissection includes the distal part of the prostate in male and vagina in female. Posteriorly the rectosacral ligament is opened to enter into the supralevator plane. Then, depending of the quality of the exposure, the sheet of the pelvic floor (levator ani) is incised distally to inter into the posterior intersphincteric plane. Typically, this is easier laparoscopically than during open surgery due to restricted view of the distal pelvis.

Perineal step

A Loue-Star anal retractor is used to expose the anal canal. A gauze is introduced into the rectum to avoid rectal and tumor spillage. A circular incision of the anal canal is performed 1 cm below the tumour. Both the mucosa and the muscular layer are incised to transect the internal anal sphincter. The rectum is then closed by sutures and the dissection between the internal and the external sphincters is performed by using scissors in a bloodless plane. It begins posteriorly then laterally, where the external sphincter is easier to identify, to finish anteriorly where the plane presents more adhesions. The dissection continues along the levator ani. Transanal division of the superior sheath of the pelvic floor then of the presacral Waldeyer's fascia allows reaching the abdominal dissection.

In patients receiving neoadjuvant treatment, the exact level of transection of the internal sphincter is decided before radiation and according to the distance from the anal verge, in order to avoid underestimation of the irradiated tumors and potential risk of tumour transection. ISR started at the dentate line to remove the upper half of the internal sphincter (partial or high ISR) for juxta anal tumours 3 to 4.5 from the anal verge. It started 1 cm below the dentate line, removing the whole of the internal sphincter for tumours below 3 cm from the anal verge (total or low ISR). A colonic J-pouch and a diverting loop ileostomy are associated with the hand-sewn coloanal anastomosis.

Personal results of ISR

From 1990 to 2010, of 1513 patients treated for rectal cancer at Saint-Andre Hospital, 232 underwent ISR for a low rectal cancer. Evolution of our indications and results of ISR have been previously reported. The preliminary experience included early low rectal cancer, T2 and small T3, mobile and located mainly at the posterior or lateral part of the rectum, and suggested few local recurrence and good continence in most patients [23]. Further experience included more advanced tumours, all the T3 were considered, included intra anal and anterior or circumferential lesions. Neoajuvant treatment became more aggressive, increasing the dose of irradiation and adding systematically concomitant chemotherapy [32]. With more experience, some patients with T4 disease and good responders were also included, and long term follow-up was evaluated [27]. In the following paragraph, we want to report the overall experience of the 232 patients treated by ISR during a 20-years period.

There were 155 males and 77 females, with a mean age of 63 (range 22–90) years and the body mass index was 25 (range 17–38). There were 5 uT1, 26 uT2, 182 uT3 and 19 uT4; 137 were classified uN+ and 13 M1. The tumour involved one quadrant of the rectum in 132 cases (57%), two quadrants in 67 cases (29%), three quadrants in 20 cases (9%) and four quadrants in 13 cases (5%). The mean lower edge of the tumour was at 3.6 cm (range 1–5) from the anal verge and at 0.5 cm (range −2–2) from the anal ring. In this series, 203 patients (87%) received preoperative radiotherapy (mean dose 50 Gy in 5 weeks) in association with concomitant chemotherapy (5FU + leucovorine + eloxatine) in 163 of them.

The ISR was performed by open surgery in 81 patients (first decade) and by laparoscopy in 151 patients (65%, 2nd decade). A colonic pouch was associated to the coloanal anastomosis in 170 patients (73%), whereas 62 patients had a straight anastomosis. A protective loop ileostomy was used in 217 of the 232 patients (94%). There were 163 partial and 69 total ISRs.

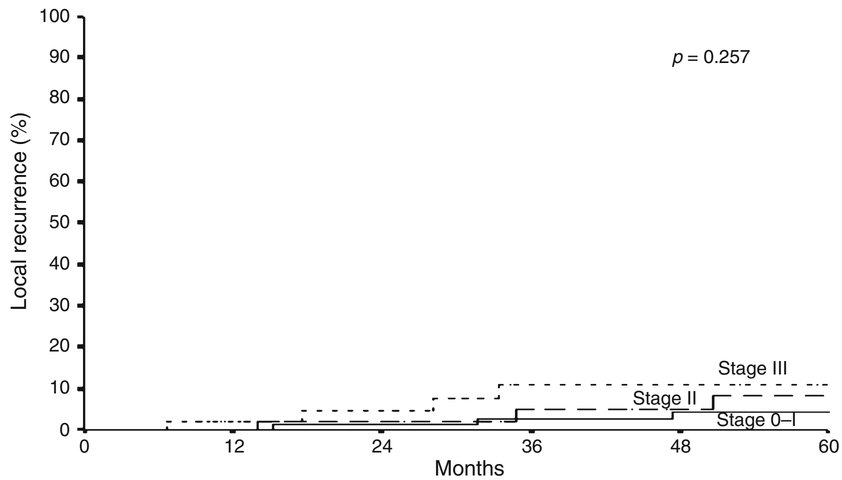

Fig. 2. Local recurrence after intersphincteric resection according to tumour stage

Oncologic results

Operative mortality included one patient (0.4%). Surgical morbidity (Dindo III–V) was 20% ($n = 46$), related with anastomotic leakage or pelvic abscess in 12% ($n = 27$). Hospital stay was 11 (range 4–76) days. Specimen assessment showed 15 stage 0 (6.5%), 87 stage I (37.5%), 56 stage II (24.1%), 61 stage III (26.3%) and 13 stage IV (5.6%). The median number of lymph nodes analyzed was 12 (range 0–32). The median distal resection margin was 15 (0–40) mm and was safe in 217 patients (94%). The median circumferential resection margin was 5 (0–18) mm and was safe (>1 mm) in 206 patients (89%). Overall, the rate of R0 resection was 86%, whereas the rate of R1 resection (positive distal or circumferential margin) was 14%. After surgery, 87 patients (38%) received postoperative adjuvant chemotherapy (6 months of 5FU + Eloxatine) due to positive lymph nodes (pN1). Three patients had a complementary APR for R1 resection.

The oncologic outcome was analyzed in the 219 patients without synchronous metastatic disease. The median follow-up was 61 (1–203) months. The crude rate of local recurrence was 5% ($n = 11$). It occurred alone in 5 patients and in association with metastases in 6 patients. R1 resection and tumour stage did not influence significantly the rate of local recurrence (Fig. 2), probably due to the low number of events. The rate of distant metastases at 5 years was 22%; it was 11% for stage I, 16% for stage II and 44% for stage III ($p < 0.001$). At 5 years, the overall and disease-free survival was 85% and 71%, respectively. Independent factors of disease-free survival after ISR were tumour stage (Fig. 3) and R1 resection. We therefore conclude that after ISR for low rectal cancer, first the main predictive factor of survival is tumour stage, second R1 resection compromises survival mainly due to distant and not local recurrence. ISR can

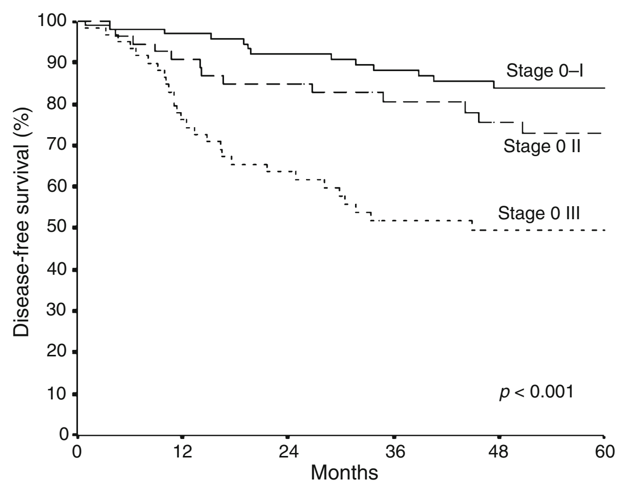

Fig. 3. Disease-free survival after intersphincteric resection according to tumour stage

therefore be proposed in all stages of low rectal cancer, including for locally advanced disease. Neoadjuvant treatment is; however, necessary to optimize local control.

Functional results

Functional outcome has been previously reported [33, 34]. First, we compared ISR with conventional coloanal anastomosis (CAA), i.e. without internal sphincter excision [33] and observed no difference in stool frequency, fragmentation, urgency, dyschesia and alimentary restriction between both techniques. However, patients with ISR had significantly worse continence (Wexner score 10.8 *vs.* 6.9; $p < 0.001$) and needed more antidiarrheal drugs (60 *vs.* 35 percent; $p = 0.04$) than patients without ISR. A good continence (perfect continence or flatus leak, Kirwan stages I–II) was present in 53% of patients after

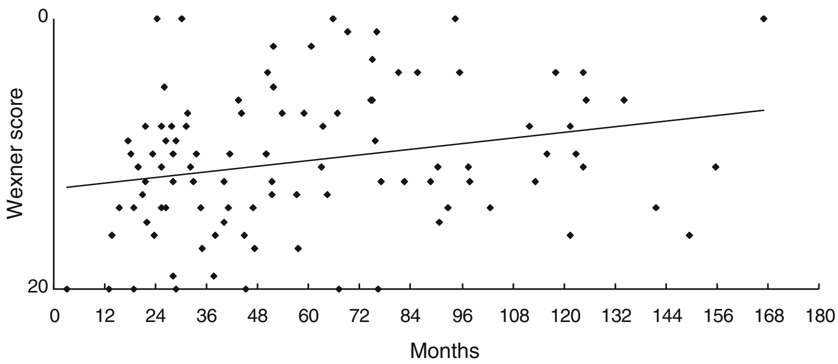

Fig. 4. Evolution of anal continence score after intersphincteric resection

ISR compared to 81% after CAA. After ISR, 35% of patients suffered from occasional leak and 12% from major leak. Clearly, as also observed in other teams [35, 36]. ISR exposes to a risk of faecal incontinence, compared to low anterior resection or conventional coloanal anastomosis.

A more recent evaluation with longer follow-up assessed predictive factors of good continence [34]. We observed that patient characteristics (age, sex and body mass index) and neoadjuvant treatment (preoperative radiotherapy) had no impact on functional outcome. Only the distance of the tumour and the anastomotic from the anal verge were independent predictors of continence. Lower the anastomosis, higher the risk of anal incontinence. This is concordant with some series showing a worse continence after total than partial ISR [35]. Although it is well admitted that pelvic irradiation is associated with a worse functional outcome [37], we were not able to demonstrate such effect probably because most of our patients (87%) received radiotherapy. Very interestingly, we observed that functional outcome, especially faecal continence score, did not alter with time (Fig. 4) suggesting that the technique of ISR is not a contra indication in old patients [34].

Laparoscopic experience

The surgical principles and the indications of the laparoscopic ISR are the same than those of the open ISR [38]. A five ports technique is used. High ligation of the artery and splenic flexure are performed with Ligasure Advance or Ultracision instruments. The TME is achieved taking care of nerve preservation and the dissection is pushed as low as possible to facilitate the perineal step. Transanal ISR permits to connect the laparoscopic pelvic dissection and the rectum is extracted via the anal canal allowing sigmoid transection without minilaparotomy. A coloanal anastomosis is performed. Advantages of the laparoscopic approach are the earlier recovery and the lower rate of incisional hernia [39]. Disadvantages include the learning curve, a longer operative time, and the potential difficulty of very low pelvic dissection in some male patients. An alternative is to begin the surgical procedure by the perineal approach, which facilitates the laparoscopic step.

We analyzed 175 patients treated by ISR for low rectal cancer in our institution and compared 110 receiving the laparoscopic and 65 the open approach [40]. Almost 86% were T3 and received long course preoperative radiochemotherapy. The two groups were similar according to age, sex, body mass index, ASA score, tumor stage and preoperative radiotherapy. Postoperative mortality (zero) and morbidity (23% *vs.* 28%; $p = 0.410$) were similar in both groups. There was no difference of 5-year local recurrence (5% *vs.* 2%; $p = 0.349$) and 5-year disease-free survival (70% *vs.* 71%; $p = 0.862$) between laparoscopic and open ISR. Functional results and anal continence (Wexner score 11 *vs.* 12; $p = 0.675$) were similar in both groups. The rate of conversion (22%, 24/110) in this series of laparoscopic ISR was higher than the 15% observed in our experience of laparoscopic TME for rectal cancer [41]. This may reflect the technical difficulties to dissect laparoscopically the very distal part of the pelvis. Prostate, puborectal levator ani muscle and the anorectal junction are difficult to expose and represent the main reasons for conversion. This explains why we recommend using the perineal step first, in case of laparoscopic restorative surgery for low rectal cancer.

How to manage difficult cases?

Intraoperative difficulty

Preoperative staging may be under evaluated, especially after neoadjuvant treatment where interpretation of fibrosis is difficult. Preoperative free surgical margin at imaging can be translated to residual hard (fixed) peri tumour tissues during surgery. In this situation, the goal is to dissect in soft tissue to optimize the chance of R0 resection. If necessary, part of the levator ani muscles, or part of the external anal sphincter can be removed. Then, reconstruction of the pelvic floor is performed by using sutures. In our experience, only a few patients received such approach, which has been described by others [42].

R1 resection after ISR

During the first decade of our experience of ISR, the multidisciplinary team, especially the oncologists, recommended to perform an immediate salvage APR in case of R1 resection following a primary ISR. This strategy presented the advantage to propose more conservative surgery due to the opportunity of salvage surgery. Unfortunately, first a few patients accepted APR in case of R1 surgery, second residual tumour cells were never observed in the few specimen after secondary APR. During the second decade of ISR, we therefore decided to follow the patients and not to propose complementary surgery after R1 resection.

We recently evaluated 299 patients treated by conservative surgery for low rectal cancer and observed that, compared to R0 surgery, R1 resection (12%) was associated with a worse survival (64% *vs.* 87%; $p < 0.01$) but not with a significant higher rate of isolated local recurrence (5.3% *vs.* 2.2%; $p = 0.45$). This suggests that after optimal conservative TME, R1 resection is related to tumour aggressiveness more than insufficient surgical excision. This concept reinforces the idea that ISR is an oncologic surgical procedure, even with very close margins, and that salvage APR is not necessary after R1 resection [43]. These results must, however, be confirmed by others.

Faecal incontinence after ISR

Any form of faecal incontinence may occur in 30 to 50% of patients after ISR. So, it appears clearly that the main limit of ISR is functional rather than oncologic. Faecal incontinence after ISR involves many factors, as extended of internal sphincter excision, pouch reconstruction, radiotherapy and colonic motility, the latter being very difficult to anticipate before surgery. It is therefore necessary to inform the patient that ultra low conservative surgery may induce faecal incontinence.

The first intention treatment of faecal incontinence after ISR and low colonic-pouch anastomosis aims to improve colonic emptying by using bulking agents and/or glycerol-based enemas (130 ml; Normacol®, Norgine Pharma, Paris, France). The goal of the treatment is to avoid both hard stools and diarrhea and to reduce outlet obstruction. The dose of bulking agents is determined for each patient according to the daily number and consistency of stools. In case of failure, low fiber diet and loperamide are proposed in association with enemas when needed. Simultaneously, patients must benefit from biofeedback therapy to improve anal sphincter function. Biofeedback consisted in weekly exercises of anal contraction assisted by a specialized nurse. Usually, medical treatment and biofeedback improve the faecal continence score and quality of life in around 50% of the patients (personal data).

In case of medical treatment failure, we tested neurostimulation ($n = 3$) and artificial bowel sphincter ($n = 2$) without successful. Myorraphy was used with success in a few patients. Recently, an anterograde colonic washout, i.e. Malone procedure, was used with good results. Finally a conventional abdominal colostomy has been used in 5% of the cases.

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Oncologic and functional outcomes of external sphincter resection

Kazuo Shirouzu and Yutaka Ogata

Abstract

Objective: The aim of this study was to evaluate the oncologic and functional outcomes of external sphincter resection (ESR) compared with those of intersphincteric resection (ISR).

Background: Abdominoperineal resection (APR) has generally been performed in the past for very low rectal carcinomas located less than 4 cm from the anal verge. Recently, there has been increasing interest in the use of intersphincteric resection (ISR) to treat such carcinomas, since this procedure removes the internal sphincter but preserves the anus. However, the oncologic and functional outcomes of more aggressive anus-preserving technique, i.e. ESR for lower rectal cancers have not yet been adequately evaluated.

Patients and methods: The surgical procedures were performed in 70 patients who were candidates for conventional APR during the period 2000–2008. Thirty patients received ESR, and the other 40 patients received ISR. The operative procedures were classified as partial-, subtotal- and total-ISR (P-ISR, ST-ISR, T-ISR); and partial- and extensive-ESR (P-ESR, E-ESR) depending on the volume of sphincter muscle resected. The Kaplan-Meier method was used to calculate survival rate. The Kirwan grade and manometry were used to evaluate anal function.

Results: ESR procedures were performed in patients with a lower tumor, and had longer operative duration, more blood loss and lower anastomosis. We had neither mortality nor severe complications after surgery. There was local recurrence (LR) in 11.9% of patients, and a radial margin (RM) <1 mm was the most powerful independent determinant of LR ($p = 0.0047$). Comparing ESR with ISR, there was no significant difference in the local recurrence rate (7.1% *vs.* 15.4%), and recurrence-free or cancer-specific 5-year survival rates (82% *vs.* 72% 91% *vs.* 85% respectively). Anal continence was preserved in 54% of the E-ESR procedures and in approximately 80% of the P-ESR or ISR procedures.

Conclusion: ESR procedures have acceptable oncological outcomes. More aggressive preoperative treatment including chemoradiotherapy is important to achieve a safe RM and to control LR. Some modification of the E-ESR procedure is needed to improve anal function.

Introduction

The anus-preserving operation such as low (or ultra-low) anterior resection (LAR) and conventional coloanal anastomosis (CAA) has become the standard treatment for lower rectal cancer. However, abdominoperineal resection (APR) has generally been performed for very low rectal carcinomas located less than 4–5 cm from the anal verge. Recently, there has been increasing interest in intersphincteric resection (ISR) for such carcinomas in Europe and Japan [1–9], since this procedure preserves the anus with removal of just the internal sphincter. The authors have previously reported two types of new anus-preserving procedures in pilot studies with short-term follow-up [6]. One procedure is ISR, which salvages the anus by removing the internal sphincter, and this is similar to the procedures reported by Schiessel et al. [1, 9] and other European surgeons [2–5]. The other is an original external sphincter resection (ESR) accompanying ISR. With the introduction of these two procedures, the use of APR has dramatically decreased to only a few procedures per year at our institution. Excellent oncologic and functional outcomes of ISR have been reported by some surgeons [8–10]. However, the oncologic and functional outcomes of ESR have not yet been evaluated. Therefore, we evaluated the oncologic and functional outcomes of ESR compared with those of ISR.

Patients and methods

Patients

Seventy patients who would otherwise have been treated with APR were selected for ESR or ISR from January 2000 to December 2008. Thirty patients received ESR and the other 40 patients received ISR. One patient with poor anal function was excluded for this surgery. All patients had a primary rectal adenocarcinoma located within 5 cm from the anal verge. Preoperative chemoradiotherapy was not performed except for one patient with ISR.

Operative techniques

The rectum was mobilized until the level of the levator muscle using total mesorectal excision (TME) technique with autonomic nerve preservation. Once the hiatal ligament was divided transabdominally, then the posterior part of the anal canal was exposed. After the intersphincteric space was circumferentially dissected from the posterior part of the anal canal using electrocautery and finger, the internal sphincter was adequately dissected and divided from the external sphincter. The intersphincteric groove was easily identified by digital examination and was subsequently cut using electrocautery. If there was no suspected invasion of tumor cells into the external sphincter, then the entire internal sphincter was removed (T-ISR, Fig. 1a). With P-ISR or ST-ISR, the internal sphincter was partially or sub-totally removed at or below the dentate line. Total or subtotal ISR (T-ISR or ST-ISR) was similar to the procedures previously described by Schiessel et al. [1, 9]. A safe distal resection margin of a least 1.0 cm was created if possible. When ESR was selected for lower tumors with suspected invasion into the external sphincter (Fig. 1b), a 1-cm wide section of the puborectal muscle was transabdominally excised until the fatty tissue of the ischiorectal fossa was sufficiently exposed. The puborectal muscle was excised partially, unilaterally or extensively, and then either P-ESR or E-ESR was accomplished by transanal dissection. ESR included removal of the entire internal sphincter combined with resection of the deep and superficial parts of the external sphincter. When the tumor was found to be confined to only one side (unilateral), then P-ESR was performed on the ipsilateral side and ISR on the contralateral side of the tumor. The anal orifice was closed to prevent dissemination of cancer cells into the pelvic cavity. After the dissection was advanced into the intersphincteric space (plane) and towards the lateral parts from the posterior side of the anal canal, the rectum was drawn out of the anus leaving the anterior part (Fig. 2a, b). When the anterior part of the anal canal was completely dissected from the prostate or vagina, similar to what is done in APR (Fig. 2c, d), the rectum and anal canal were entirely removed. Finally, the coloanal anastomosis was performed with 3-0 Vicryl sutures after pulling the sigmoid colon down to the anus without tension (Fig. 3a, b), as previously described by Parks et al. [11]. An end-to-end straight anastomosis or a 5–6 cm colonic J-pouch anastomosis was performed in ESR, and in ISR. A diverting loop ileostomy was performed in all patients.

Oncologic assessment and selection of the operative procedure

Routine preoperative oncologic assessment included digital examination, barium enema, rigid proctoscopy, computed tomography (CT) and/or magnetic resonance imaging (MRI). When a tumor was relatively small, then endorectal ultrasonography was used to estimate the tumor spread. Our previous pathological pilot study showed that the extent of invasion into the external

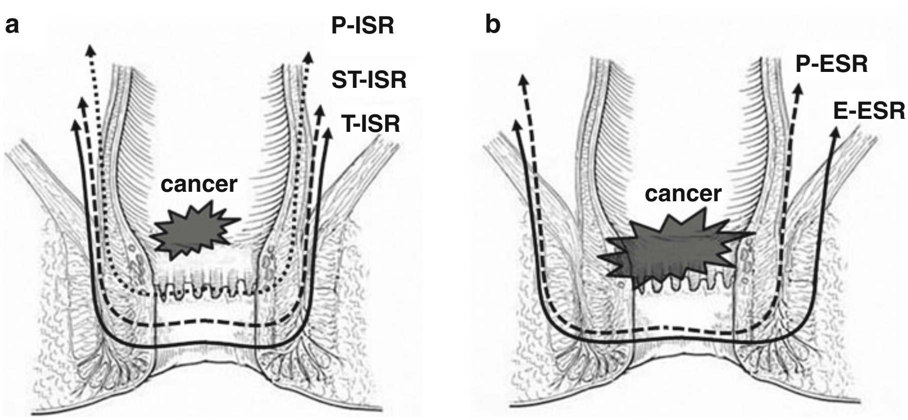

Fig. 1. Schema of the ISR and ESR procedures. (**a**) With T-ISR, entire internal sphincter is removed. With P-ISR or ST-ISR, the internal sphincter was partially or sub-totally removed at or below the dentate line. (**b**) With ESR, the entire internal sphincter was removed combined with external sphincter resection of the deep and superficial parts. When the tumor was confined to only one side (unilateral), then P-ESR was performed on the ipsilateral side and ISR on the contralateral side of the tumor. *P-ISR* Partial intersphincteric resection; *ST-ISR* subtotal intersphincteric resection; *T-ISR* total intersphincteric resection; *P-ESR* partial external sphincter resection; *E-ESR* extensive external sphincter resection

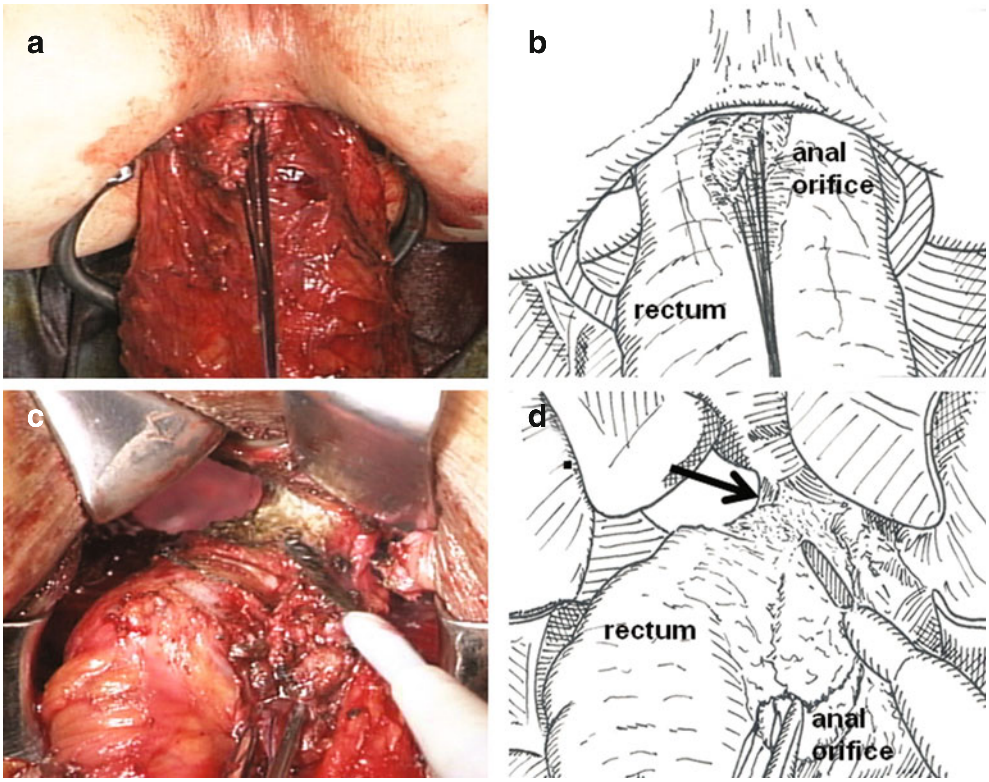

Fig. 2. Perineal procedures. (**a**, **b**) The rectum is drawn out of the anus leaving the anterior part. (**c**, **d**) The anterior part of the anal canal (*arrow*) is dissected from the prostate or vagina, similar to what is done in abdominoperineal resection (APR)

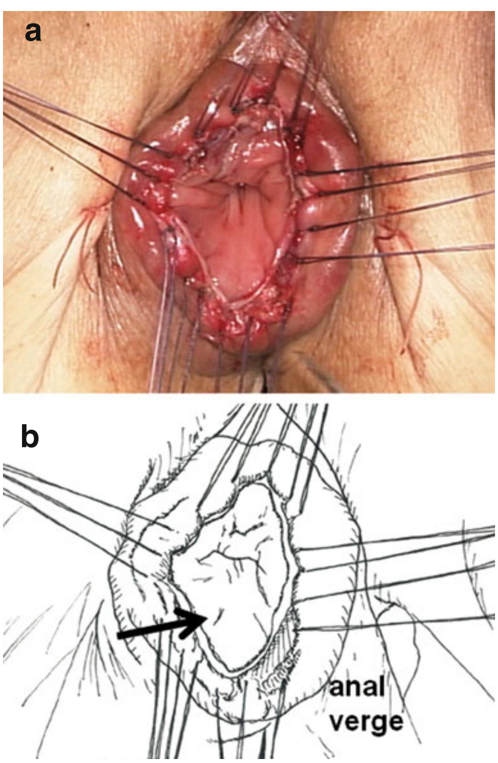

Fig. 3. Coloanal anastomosis. (**a**, **b**) The coloanal anastomosis is performed with 3-0 Vicryl sutures after pulling the sigmoid colon (arrow) down to the anus without tension

sphincters was low (less than 10%) when the tumor was located above the dentate line but the extent was detected at a higher rate (approximately 40%) when the tumor was located at or below the dentate line [12]. Based on the pilot study, the surgical indication for ESR or ISR was determined preoperatively by digital examination to judge the tumor location, and then the extent of invasion into the external sphincters was confirmed using CT and/or MRI. When a tumor was freely mobile under digital examination and there was no invasion into the external sphincters based on CT and/or MRI, then ISR was used for most tumors that were located completely above the dentate line. When CT and/or MRI suggested invasion into the external sphincters except for the subcutaneous part, then ESR (P-ESR, E-ESR) was selected for some lower tumors that were located at or below the dentate line. Finally, the appropriate treatment was selected after digital examination under general anesthesia or by transabdominal palpation during the operation.

Functional assessment

Assessment of anal function was performed before and at 3 months after the first operation, and then at 3, 6 and 12 months after ileostoma closure. The continence status of each patient was evaluated using the standardized classification proposed by Kirwan et al. [13]. Physiologic assessment was performed based on a manometric study using an anorectal function testing kit (GMMS Gastrointestinal Manometry System: GMMS-200, Star Medical, Tokyo, Japan). Maximum resting pressure (MRP) and maximum squeeze pressure (MSP) were measured before and at 3 months after the first operation, and then at 3, 6 and 12 months after ileostoma closure.

Postoperative follow-up

All patients were followed in outpatient visits and routine investigations were performed. The most recent date of contact was regarded as the final date of confirmation in each case. The overall final follow-up date for this study was the last day of December 2010. The postoperative surveillance included measurement of tumor markers, chest radiography and ultrasonography every 3 months for the first year, every 3 to 6 months for the next four years and then annually thereafter. Chest and abdominal CT and/or MRI were performed as needed if there was any suspected site of recurrence. In the absence of any suspected recurrence, these imaging procedures were performed every 6 months for the first 3 years, and then annually thereafter. The median follow-up duration of the surviving patients was 50 months (range, 12–111 months). The first site of recurrence was recorded for each patient and defined as distant metastases or as local (intra-pelvic) recurrence including the pelvic floor or pelvic lymph nodes.

Statistical analysis

Student's *t*-test, the Chi-square test, Fisher's exact test or the Mann-Whitney *U*-test were used to determine the statistical significance of any differences among the procedures. The Kaplan-Meier method was used to calculate survival rates. The significance of differences in survival rates among the procedures was assessed using the log-rank test. Multivariate Cox regression analysis was performed to determine the risk factors that were independent determinants of local recurrence (LR). A *p*-value <0.05 was considered significant.

Table 1: Preoperative characteristics of the patients and tumors

Characteristics	ESR [$n=30$]	ISR [$n=40$]	*p*-value
Age (years)*	65 (32–82)	64 (36–82)	n.s.
Gender (M/F)	19/11	20/20	n.s.
Body weight (kg)*	56 (38–74)	55 (36–76)	n.s.
BMI (kg/m^2)*	22 (17–32)	22 (16–29)	n.s.
CEA (ng/ml)*	6 (0.7–5612)	4.7 (0.5–231)	n.s.
Size of tumor (mm)*	50 (30–125)	39 (15–140)	0.043
Distance from DL (mm)*	5 (−10–25)	13 (−5–25)	0.006
Distance from AV (mm)*	20 (10–45)	30 (15–50)	0.005
Preoperative radiation (yes/no)	0/30	1/39	n.s.

*Values are median (range). *BMI* Body mass index; *CEA* carcinoembryonic antigen; *DL* dentate line; *AV* anal verge; *n.s.* not significant.

Table 2: Surgical outcomes after ESR and ISR

Characteristics	ESR [$n=30$]	ISR [$n=40$]	*p*-value
Reconstruction (S/JP/CP)	17/13/0	27/12/1	n.s.
Anastomosis from AV (mm)*	7.0 ± 3.9	11.9 ± 4.5	<0.0001
Diverting ileostomy (yes/no)	30/0	40/0	n.s.
Blood loss (ml)**	587 (300–1500)	400 (105–2500)	0.0011
Transfusion (yes/no)	4/26	6/34	n.s.
Pelvic node dissection (yes/no)	11/19	4/36	0.0093
Operative duration (min)**	428 (240–645)	360 (225–610)	0.0019
Curative surgery (yes/no)	28/2	39/1	n.s.
Mortality (yes/no)	0/30	0/40	n.s.
Complications (yes/no)	10/20	5/35	n.s.
Anastomotic leakage (yes/no)	3/27	2/38	n.s.
Anovaginal fistula (yes/no)	1/29	0/40	n.s.
Anastomotic stenosis (yes/no)	3/27	0/40	n.s.
Colonic necrosis (yes/no)	1/29	0/40	n.s.
Pelvic abscess (yes/no)	3/27	1/39	n.s.
Ileus (yes/no)	0/30	1/39	n.s.
Others (yes/no)	0/30	1/39	n.s.

*Values are mean ± SD, **Values are median (range). *n.s.* not significant; *ESR* external sphincter resection; *ISR* intersphincteric resection; *S* straight; *JP* J-pouch; *CP* coloplasty; *AV* anal verge.

Results

Preoperative characteristics of the patients and tumors

There was no significant difference concerning age, gender, body weight, BMI, and CEA between ESR and ISR (Table 1). ESR was performed for larger and lower tumors compared with ISR.

Surgical outcomes

As shown in Table 2, 30 patients underwent ESR (P-ESR in 17 and E-ESR in 13), and 40 patients underwent ISR (T-ISR in 28, ST-ISR in 7 and P-ISR in 5). ESR procedures had lower anastomosis, more blood loss, higher rate of pelvic lymph node dissection, and longer operative duration with significance compared to ISR procedures. There were no operative or in-hospital death in patients with ESR and ISR. There was no significant difference concerning others characteristics between both procedures.

Pathological outcomes

The postoperative pathological outcomes are listed in Table 3. Intersphincteric space invasion was detected at a significantly higher rate (36.7%, $p = 0.0052$) in the surgical specimens treated with ESR. Barium enema shows a case of lower rectal cancer treated with ESR (Fig. 4a). Surgical specimen shows intersphincteric space (ISS) invasion and some cancer cells are seen just above the external sphincter muscle (ESM) (Fig. 4b). In contrast, the invasion was rarely identified (7.5%) in the ISR specimens. Resection with a radial margin (RM) ≤1 mm (RM1) was detected in 20% with ESR, and in 10% with ISR, and the difference between the two groups was not significant. No significant difference was observed in tumor differentiation, lymphovascular invasion or pTNM stage between ESR and ISR.

Table 3: Pathological outcomes after ESR and ISR

Characteristics	ESR [$n = 30$]	ISR [$n = 40$]	p-value
Differentiation (well/mod-others)	15/15	23/17	n.s.
Lymphatic invasion (ly0–1/ly2–3)	22/8	36/4	n.s.
Venous invasion (v0–1/v2–3)	24/6	38/2	n.s.
Intersphincteric space invasion	11 (36.7%)	3 (7.5%)	0.0052
Radial margin (RM) ≤1 mm	6 (20%)	4 (10%)	n.s.
pTNM 6th (0–I/II/III/IV)	6/16/6/2	14/11/14/1	0.095

ESR External sphincter resection; *well* well differentiated adenocarcinoma; *mod* moderately differentiated adenocarcinoma; *ly0-1, v0-1* negative to minimal invasion; *ly2-3, v2-3* moderate to severe invasion; *n.s.* not significant.

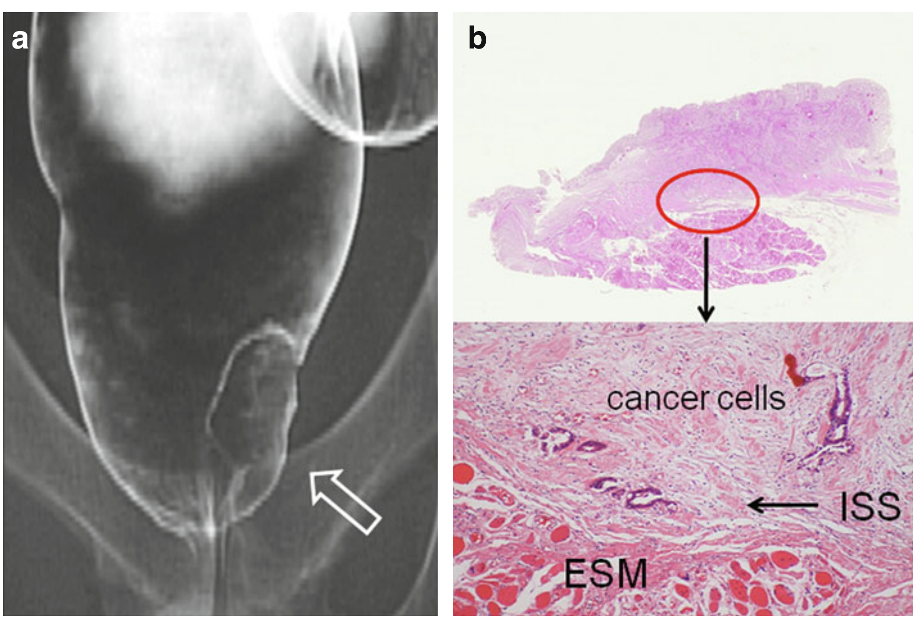

Fig. 4. A case of lower rectal cancer treated with ESR. (**a**) Barium enema shows a tumor (arrow) whose lowest edge is located below the dentate line. (**b**) Surgical specimen shows intersphincteric space (ISS) invasion. Some cancer cells are seen just above the external sphincter muscle (ESM)

Oncologic outcomes

Sixty-seven patients with curative surgery were analyzed for oncologic outcomes (Table 4). Postoperative recurrence developed in 17.9% after ESR and in 25.6% after ISR. Distant metastasis occurred in 7.1% after ESR and in 10.3% after ISR. Total LR including the pelvic floor and/or pelvic lymph node metastasis was detected in 8 patients (11.9%) including 2 patients (7.1%) after ESR and 6 patients (15.4%) after ISR. A multivariate Cox regression analysis showed that RM1 was the most powerful independent risk factor for LR ($p = 0.0047$, Table 5). The 5-year recurrence-free survival rate was 82% after ESR, and 72% after ISR. The 5-year cancer-specific survival rate was 91% after ESR, and 85% after ISR. There was no significant difference in either survival rate between the ESR and ISR groups (Fig. 5).

Functional outcomes

The continence status according to Kirwan et al. [13] is shown in Table 6. Excellent continence (Kirwan grade I or II) was found in 54% of E-ESR, in 80% of P-ESR and in 77% of ISR patients ($p = 0.087$). Frequent major soiling (Grade IV) occurred in 31% of E-ESR patients. No patient had Grade V incontinence.

Table 5: Multivariate Cox regression analysis for local recurrence

Independent variable		HR	95% CI	*p*-value
Size of tumor	>50 mm	0.914	0.152–5.508	0.9219
Histology	Except well	2.607	0.549–12.391	0.2281
Lymphatic invasion	ly2-3	0.832	0.054–12.879	0.8955
Venous invasion	v2-3	10.81	0.543–215.23	0.1188
Perineural invasion	Yes	9.891	1.239–78.954	0.0306
Operative method	ESR	0.422	0.038–4.707	0.4829
Pelvic LN dissection	Yes	0.476	0.048–4.691	0.5245
LN metastasis	Yes	1.92	0.222–16.575	0.5531
RM1	Yes	9.313	1.985–43.692	0.0047

HR Hazard ratio; *CI* confidence interval; *ESR* external sphincter resection; *LN* lymph node; *RM1* radial margin ≤1mm.

Table 4: Oncologic outcome after curative surgery

Recurrence	ESR [$n = 28$]	ISR [$n = 39$]	Total [$n = 67$]	*p*-value
Local	2 (7.1%)	6 (15.4%)	8 (11.9%)	n.s.
Distant	2 (7.1%)	4 (10.3%)	6 (9.0%)	n.s.
Local + Distant	1 (3.6%)	0	1 (1.5%)	n.s.
Total	5 (17.9%)	10 (25.6%)	15 (22.4%)	n.s.

ESR External sphincter resection; *ISR* intersphincteric resection.

Table 6: Functional outcome at 12 months after ileostoma closure

Kirwan grade	E-ESR [$n = 13$]	P-ESR [$n = 15$]	ISR [$n = 34$]	*p*-value
I	4 (31%)	10 (67%)	22 (65%)	0.087
II	3 (23%)	2 (13%)	4 (12%)	
III	2 (15%)	2 (13%)	7 (21%)	
IV	4 (31%)	1	1	
V	0	0	0	

E-ESR Extensive external sphincter resection; *P-ESR* partial (unilateral) external sphincter resection; *ISR* intersphincteric resection.

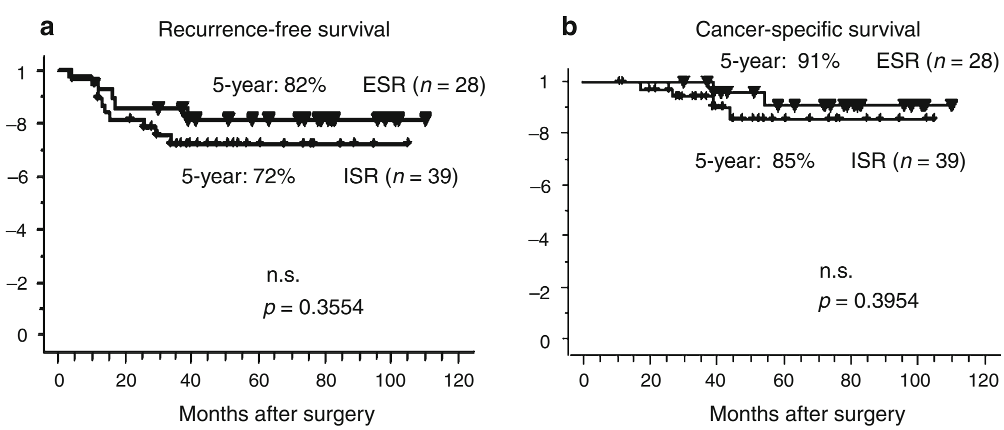

Fig. 5. Survival curves after ESR and ISR. (**a**) The 5-year recurrence-free survival rate was 82% after ESR and 72% after ISR. (**b**) The 5-year cancer-specific survival rate was 91% after ESR and 85% after ISR. There was no significant difference in survival rates between ESR and ISR. *ISR* Intersphincteric resection, *ESR* external sphincter resection

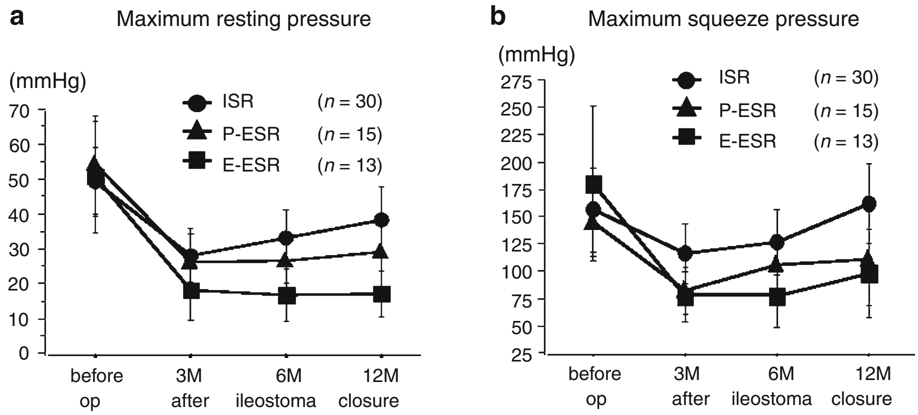

Fig. 6. Manometry. (**a**) The maximum resting pressures in patients with ISR and P-ESR at 12 months after ileostoma closure were significantly higher than that in patients with E-ESR (E-ESR *vs.* ISR, $p = 0.0037$; E-ESR *vs.* P-ESR, $p = 0.0453$; Mann-Whitney *U*-test). (**b**) The maximum squeeze pressure in patients with ISR at 12 months after ileostoma closure was significantly higher than that in patients with E-ESR (E-ESR *vs.* ISR, $p = 0.0469$, Mann-Whitney *U*-test). *ISR* Intersphincteric resection; *P-ESR* partial external sphincter resection; *E-ESR* extensive external sphincter resection

The results of manometry are shown in Fig. 6. Manometric pressure measurements before the first operation, and at 3, 6 and 12 months after ileostoma closure were performed in 13 patients with E-ESR, in 15 with P-ESR and in 30 with ISR. The MRP in the patients with ISR and P-ESR was significantly higher than that in patients with E-ESR at 12 months after ileostoma closure ($p = 0.0037$ and $p = 0.0453$, respectively). The MSP in patients with ISR was significantly higher than that in patients with E-ESR at 12 months after ileostoma closure ($p = 0.0469$).

Discussion

In our institution, APR has generally been performed for lower rectal cancers located within 4–5 cm from the anal verge for the past 20 years; however, the use of APR has dramatically decreased since ISR was launched in 2001. One important concern with ISR is whether a safe surgical margin can be obtained. It appears that a least 1 cm distal resection margin is sufficient in most cases of rectal cancer [14, 15]. Regarding radial spread of the tumor, our postoperative pathological data showed that the intersphincteric space invasion occurred at a significantly higher rate of 36.7% with the ESR procedure (Table 3). Cancer cells were frequently found on the surface of the external sphincter in the surgical specimens treated with ESR (Fig. 4). This is because the ESR procedure was performed in the lower tumors located at or below the dentate line, that was compatible with the concept of the previous pathological pilot study [12]. If ISR were selected for such patients, then the radial margin might be exposed to tumor cells. That is why we have aggressively performed ESR. When the tumor is confined to a limited area with suspected external sphincter invasion, then P-ESR is carefully performed on the ipsilateral side, and ISR on the contralateral side of the tumor. Holzer et al. [16] suggested that APR should be performed in patients with external sphincter invasion. However, the ESR technique allows us to preserve the anus in such patients.

Local tumor control is another concern. Although RM1 was detected at a rate of 20% even with ESR, the LR rates after ESR and ISR were 7.1% and 15.4%, respectively. These values are not much different from the values reported in other series (2–10%) [4, 9, 17, 18]. Acceptable local tumor control could be achieved without chemoradiotherapy (CRT) by either ESR or ISR. However, since a RM1 was the most powerful independent risk factor for LR ($p = 0.0047$), it is possible that preoperative CRT may decrease the risk of RM1. Preoperative CRT induced tumor down-staging, including distal and radial margins in patients who underwent ISR [10]. Preoperative CRT may increase the probability of anus preservation by either ESR or ISR and may keep the radial margin free from disseminating cancer cells. However, impaired anorectal function with preoperative CRT [19] has increased the need for permanent stoma [20] and has shown no survival benefit [21, 22]. Further investigation is warranted in patients undergoing ESR or ISR to determine the efficacy of preoperative CRT.

The 5-year recurrence-free and cancer-specific survival rates in our series were 80–90%, which are similar to the reported overall survival rates in ISR patients [1, 18]. Japanese oncologic outcomes, based on a multicenter investigation that included our institution, showed that ISR was associated with almost the same LR rate (5.8%), 5-year overall survival rate (91.9%) and 5-year disease-free survival rate (83.2%) [23]. Our oncologic outcomes are acceptable according to these results.

As for defecation symptoms, approximately 80% of patients with either ISR or P-ESR had good continence (Kirwan grade I or II), which is similar to that reported in other series [1–3]. Some patients with either ISR or P-ESR complained of occasional night soiling and used pads. It was not surprising that poor continence (Kirwan grade IV) and the lowest level of manometric pressure would occur most often in patients with E-ESR. Our results showed that preservation of the external sphincter was strongly related to the improvement of anal function. Although it has been shown that colonic J-pouch anastomosis achieved better function compared with straight anastomosis [24], we usually do not perform J-pouch anastomosis in obese patients.

MRI seems to be extremely important in the preoperative selection of the surgical strategy. Some authors have reported that MRI was valuable for predicting the extent of invasion into the anal canal structures [25, 26]. Even though we use MRI, CT and barium enema to visualize tumors preoperatively, careful intraoperative digital examination, transabdominal palpation and observation are very important to select the optimal procedure and ensure a successful outcome.

In conclusion, both ESR and ISR are reasonable techniques for very low rectal carcinomas. These operative techniques are an alternative surgical option to APR. However, E-ESR requires further evaluation of postoperative anal function. To achieve a safe RM and to control LR, appropriate preoperative treatment including CRT should be considered.

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Intersphincteric resection for very low rectal cancer

Special reference to surgical techniques

Yoshihiro Moriya

Introduction

Goals for rectal cancer surgery include complete tumor resection to minimize the risk of relapse and maintenance of quality of life. Local control and survival of patients with rectal cancer have improved with the development of surgical techniques and combined adjuvant therapy. The advent of double-stapling techniques and coloanal anastomosis has facilitated the construction of very low rectal anastomosis.

Historically and practically, decision-making is related to the distance from the lower edge of tumor to the anal canal. This is because of the potential risk of both intramural and mesorectal microscopic spread below the tumor. Therefore, at least 5 cm of distal margin was required until the 1980s [1], after which 2 cm was considered adequate [2]. In fact, it is not technically possible to obtain a 2 cm distal margin by using conventional abdominal approach in patients with rectal tumors located below 5 cm from the anal verge, because the median length of the anal canal is 3 to 4 cm. Furthermore, to obtain an adequate radial margin with sphincter preservation in very low rectal cancer is not certain. Therefore, for both technical and oncological reasons, it is generally accepted that most rectal cancers less than 5 cm from the anal verge (AV) or less than 2 cm from the dentate line (DL) are treated by using abdomino-perineal resection (APR).

However, recent studies have shown that a margin of more than 2 cm is not necessary to prevent local recurrences, and a distal margin of 1 to 2 cm is now considered sufficient in most instances, with local recurrence rates of 4 to 13 percent [3–5].

Considering the above-mentioned background, intersphincteric resection (ISR) with coloanal anastomosis has been proposed to avoid permanent colostomy for rectal cancers located less than 5 cm for the AV by a few specialized teams [5–7].

The goal of ISR is to divide the rectum transanally and to remove part or the whole of the internal anal sphincter, to obtain both adequate distal and radial margin in order to prevent a permanent colostomy. A more modern concept focuses on the radial margin more than the distal margin [6, 8, 9]. In other words ISR can be an alternative to APR for selected rectal tumors situated at the anorectal junction, without compromising oncological outcomes.

Anatomy of the anal canal (Fig. 1)

It is obligatory to know the anal anatomy very well in order to carry out ISR precisely. The surgical anal canal can be defined as the distance between the anorectal ring and the AV. The intersphincteric groove can be palpable as a little hollow by careful digital examination. The cranial portion of intersphincteric groove becomes narrow and cylindrical with a length of 3 to 4 cm. After passing this narrow portion, the upper edge of anorectal ring, which is defined by the sling of muscle forming the anal hiatus of the pelvic diaphragm can be palpated. The anorectal ring is corresponding to the superior margin of puborectalis muscle attachment. It is called alias Herrmann's line. The mesorectum is thin or lacking at this level. The inner circular muscle becomes increasingly thicker, to constitute the non-striated internal sphincter muscle. The external sphincter is a trilaminar striated muscle. At the lower extremity of the rectum, the outer longitudinal rectal muscle fibers fuse with the striated muscle fibers from the levator ani muscle and fibro-elastic tissue from the supra-anal fascia to form the conjugated longitudinal muscle of the anal canal, which radially extends into the trilaminar external sphincters.

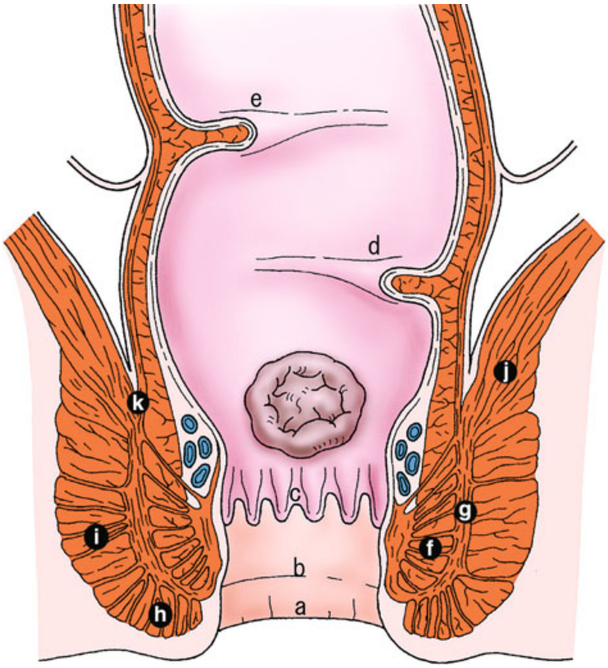

Fig. 1. Anatomy of anal canal; (**a**) anal verge (AV); (**b**) intersphincteric groove; (**c**) dentate line (DL); (**d**) lower Houston valve; (**e**) middle Houston valve; (**f**) internal sphincter muscle; (**g**) conjoined longitudinal muscle; (**h**) subcutaneous external sphincter muscle; (**i**) deep external sphincter muscle; (**j**) puborectalis muscle; (**k**) anorectal ring; from a to k: length of the surgical anal canal

The levator ani muscle is assumed to be composed of three individual components; the puborectalis, pubococcygeus and iliococcygeus muscles. The puborectalis muscle is the most medial portion of the levator muscle. Both levator ani and external sphincter muscle pull the lower part of rectum and anal canal anteriorly to create the anorectal angle, which plays a crucial role in defecation function. ISR is an ultimate sphincter-preserving procedure by removing the whole rectum and partial or whole internal sphincter. Total ISR or low ISR involves complete excision of the internal sphincter for tumors spreading to or beyond the DL. The distal cut-end line is at the intersphincteric groove. Total ISR is unnecessary in patients with tumor located more than 2 cm from the DL. Those patients undergo partial ISR or high ISR, in which the distal cut-end line is between the DL and intersphincteric groove. Although a partial ISR in patients with a wide pelvis can be carried out through an abdominal approach, transanal approach appears to be the optimal way for ISR. This is, because the dissection is better visible anatomically, and allows a more accurate evaluation of the lower edge of tumor, even in patients with a difficult narrow and deep pelvis. Anatomically, ISR is based on the concept that if one follows the muscular tube of anorectum distally, one eventually exits on the anoderm in the intersphincteric groove at the anal verge [4].

Patient selection

ISR is indicated for patients with well to moderately differentiated adenocarcinomas located either just above or just below the anorectal ring which have not invaded the external sphincter or the pelvic floor. In the presence of anterior-lying tumors, it may be advisable to evaluate depth of invasion more precisely with MRI plus endoanal ultrasonography whether or not the external sphincter is involved. Urban [11] used double-contrast, material-enhanced MRI with a flexible surface coil and reported a specificity of 98% and sensitivity of 100% in assessment of anal sphincter infiltration.

Careful consideration of the indication for ISR is necessary to prevent the following: (1) Increased risk of relapse, especially local recurrence (2) Implantation of exfoliated cancer cells in the operative field, especially in trans-anal phase (3) Impaired defecation function. ISR can be considered in patients who are strongly opposed to a permanent colostomy and who have consented to prolonged close follow-up. Patients should be screened to have adequate sphincter function preoperatively, assessed by interview, digital examination or, better yet, by manometric study. They should thoroughly understand the uncertainties of postoperative defecation control and the need to have patience during the early months after the operation [5–7]. Contraindications of ISR include patients with invasion of external sphincter or levator ani muscle, and those with fixed tumors or synchronous metastases.

Patient with T3 disease or those with T2 disease with infiltration of the internal sphincter should be considered to receive neoadjuvant chemoradiation therapy to obtain downstaging in order to maximize surgical margins and to avoid intra-operative tumor seeding [6, 12].

Surgical techniques

The surgical technique includes both abdomino-pelvic and perineal approaches.

Abdominal approaches

The surgeon stands on the patient's left side after the patient is placed in lithotomy position using Levitator. A long midline incision is made starting just above the symphysis and extending to the umbilicus and around it on the left side to provide easy access to the splenic flexure. The intra-abdominal cavity is inspected and the liver is palpated for existence of possible metastasis. If resection is possible the sigmoid is exposed by retraction of the small intestines behind wet gauzes. An incision of

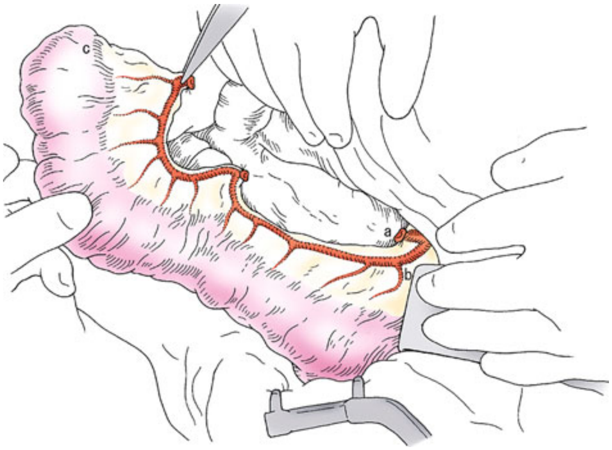

Fig. 2. Creation of colonic stump for anastomosis: no tension and adequate blood supply confirmed by pulsation of the marginal artery; (**a**) stump of superior rectal artery; (**b**) preserved left colonic artery; (**c**) colonic stump for anastomosis

the peritoneum is made down the left lumbar gutter. The peritoneum is lifted up until the left gonadal vessels and the ureter are identified throughout their course down over the pelvic brim.

The inferior mesenteric artery and vein may usually be ligated distal to the origin of the left colic artery or at its point of origin from the aorta in patients with a thickened sigmoid mesocolon or a short sigmoid colon. The blood supply to the colon must now come from the middle colic artery through the marginal vessels of Drummond. The splenic flexure is mobilized and the sigmoid or descending colon is transected. During the downward dissection, the superior hypogastric plexus (SHP) and paired hypogastric nerves (HN) below the aortic bifurcation should be identified and preserved. In order to construct a stable anastomosis a good technique, no tension and adequate blood supply confirmed by pulsation of the marginal artery is necessary (Fig. 2). The surgeon must now determine whether the rest of the colon is sufficiently mobile to be brought down beyond the pubic symphysis for a coloanal anastomosis without tension. In order to accomplish this, it may be necessary to divide the lateral peritoneal attachment of the left colon up to and including the splenic flexure. The length of sigmoid colon is subject to great variations. Unless the sigmoid is very long, usually the left half of the transverse colon along with the splenic flexure must be mobilized. For patients undergoing ISR, a 5- to 6-cm colonic J-pouch is selectively created, based on anatomic limitations and the surgeon's preference [13]. If there is insufficient intestinal length, a restrictively narrow pelvis, or an excessively bulky descending colonic mesentery, a straight end-to-end coloanal anastomosis is generally performed. A temporary diverting ileostomy is used at the discretion of the surgeon.

Pelvic approaches

The peritoneum is incised down to Douglas on the left side. The next important step is the visualization of the left ureter throughout its course over the pelvic brim and down to the bladder. The ureter will respond with peristaltic waves after it is pinched with forceps. The next is the right side of the rectosigmoid. The right ureter is identified beneath the residual peritoneum. It is important at this point to identify and isolate both ureters and the gonadal vessels.

The intrapelvic rectal dissection by using the TME technique should be carried out in defined anatomic planes, under direct vision using sharp dissection. Rectal mobilization in the pelvis is composed of the following three steps. The first step consists of identification of the paired HN and dissecting in the loose retrorectal space, up to the bottom of sacral flexure and identification of the Denonvilliers fascia at the anterior dissection. The second step is exposure of the inferior hypogastric plexus (IHP) at the lateral sides. The third step consists of dissection of the recto-coccygeal ligament and entering the conjugated longitudinal muscle of the anal canal at the posterior space and dissection under the prostate while preserving the neurovascular bundle (NVB) at the anterior plane.

Keeping above-mentioned steps in mind, the rectal dissection should be carried out from the sacral promontory to the anal canal. Whenever bleeding occurs, hemostasis should be performed to maintain a dry operative field in order to accurately identify each anatomical mark in the pelvis. This meticulous procedure is of great importance, especially during the dissection of deep part of the pelvis. Bleeding during the retrorectal dissection is stopped with fine silk ligatures or electrocautery.

First step of the pelvic dissection (Fig. 3)

The SHP is visualized below the aortic bifurcation. The dissection proceeds behind the superior rectal vessels toward the entrance of the presacral space above the sacral promontory, identifying and exposing the paired HN. Division of the retrorectal or sparse space along the sacral curvature in the direct vision of the middle sacral vessels beneath the parietal fascia from the sacral promontory downward to the level of third sacral bone, which is correspond to the level of recto-sacral fascia, is done sharply in the midline with long scissors or electrocautery, using a long insulated tip.

In the initial step of the anterior dissection, the peritoneal reflection of the pouch of Douglas is incised about 1 cm up to its anterior reflection over the bladder in men or

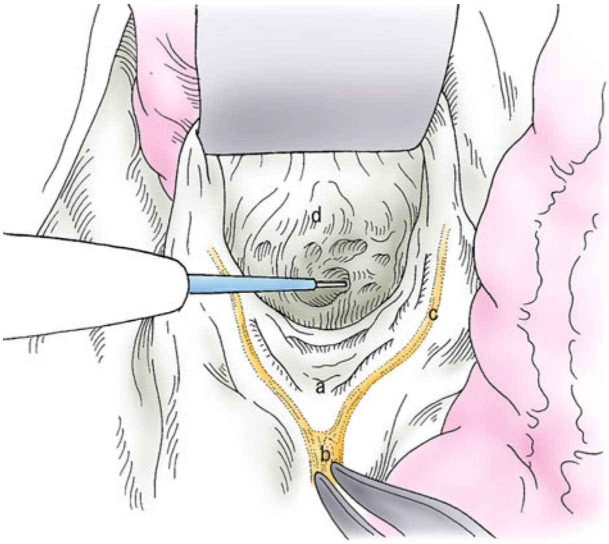

Fig. 3. Dissection of retrorectal space; (**a**) sacral promontory; (**b**) superior hypogastric plexus (SHP); (**c**) hypogastric nerve (HN); (**d**) loose retrorectal space

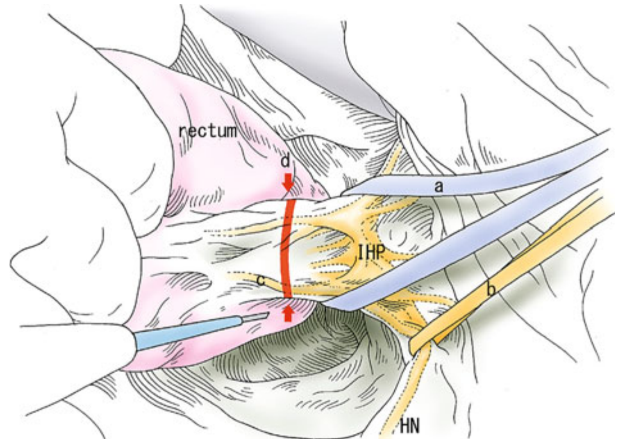

Fig. 4. Cutting line of rectal branches from the inferior hypogastric plexus (IHP): right side; (**a**) vessel loop around the inferior hypogastric plexus (IHP); (**b**) vessel loop around the hypogastric nerve (HN); (**c**) rectal branches of autonomic nerves; (**d**) red arrows show cutting line

behind the uterus in women. The bladder or uterus is retracted anteriorly using a fiberoptic lighted deep pelvic retractor. In case of T3 disease, the sharp dissection proceeds above Denovillier's fascia until the prostate and seminal vesicles or the rectovaginal septum is seen. The paths of the anterior and posterior dissections show the close adherence to the presacral fascia posteriorly and to the seminal vesicles and prostate anteriorly.

Second step of pelvic dissection (Fig. 4)

Next target is the division of lateral side of the middle rectum. When the recto-sacral fascia is sharply divided, the root of S3 pelvic nerve which is located just below the piriform muscle is identified. The posterior dissection continues down to the level of coccyx. It is very important that bleeding is minimized. Good lighting obtained by the use of the fiberoptic lighted deep pelvic retractor or headlamp is essential for clear visualization during lateral retraction of the middle rectum and anterior elevation of the bladder or uterus and vaginal. What is called the lateral ligament of the rectum is identical with the IHP. By lifting a portion where HNs mingle with IHP, some nerve branches from the plexus into the mesorectum are identified and divided by using electrocautery or sharp scissors. During this maneuver, the anatomical relations between the HN, IHP and roots of S3 and S4 pelvic splanchnic nerves are unfolded. To perform this, countertraction between the rectum and what is called the lateral ligament becomes essential. The middle rectal artery which exists in 25–55% of cases may require a ligature. The preservation of IHP and roots of S3 and S4 pelvic splanchnic nerves are essential for sexual and urinary function. The IHP (4 to 5 cm in size and flat-shaped) is seen as a dense sheet of nerve fibers that comes close to the rectum at the level of the seminal vesicle and upper prostate or upper vagina. The TME procedure does not encounter the "IHP itself" but rather branches from this nerve plexus into the lateral mesorectum.

The retrorectal space can be widely open after the completion of division of lateral sides of the rectum as the second step procedure.

After separation of the rectum from IHP, the rectum may be lifted or pulled out antero-cranially with the left hand. As of now, whether lymph node swellings in the mesorectum are present or not should be checked by a careful palpation.

Third step of pelvic dissection (Fig. 5)

On the final stage of the anterior dissection, sharp dissection should be carried out to free the rectum as low near the perineal body as possible in order to lessen the blood loss and prevent accidental injury to the urethra and NVBs during the subsequent transanal approach. The dissection has to reach the upper part of the external sphincter anteriorly, i.e. the apex of the prostate in men.

Target of the lateral dissection of the lower rectum is identification and preservation of NVBs, which include the cavernous nerve, its accompanying vessels and frequently contains rectal vessel branches while winding round the lateral wall of lower rectum. Accordingly, the NVBs are freed from the lower rectum under attention not to bleed. NVBs are potentially in danger of injury during this procedure.

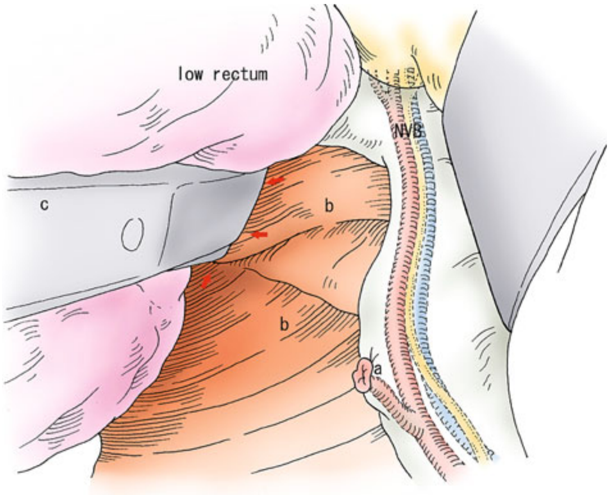

Fig. 5. Exposure of intersphincteric plane between the puborectalis muscle and the internal sphincter. NVB: neurovascular bundle including cavernous nerve; (**a**) stump of middle rectal artery; (**b**) puborectalis muscle; (**c**) long Mayo scissors; Three red arrows indicate dissecting layer between puborectal muscle and the internal sphincter

When retrorectal dissection proceeds up to the coccyx, the recto-coccygeus muscle or the so-called posterior ligament, which contains end branches of middle sacral vessels is exposed and divided. In performing APR, this ligament should be removed en-bloc. The dissection has to reach the puborectalis muscle posteriorly. Following identification of the puborectalis muscle binding the rectum at the pelvic bottom, dissection proceed as downward as possible in the conjugated longitudinal muscle between the internal and external sphincter muscle. This maneuver is assisted by using the rounded, blunt end of the long Mayo scissors. The conjugated longitudinal muscle is the right layer for ISR. During these procedures, the tumor is evaluated through gentle palpation by the surgeons. If tumor had invaded beyond the rectum into the puborectalis muscle or external sphincter at the anorectal junction or anal canal, the puborectalis muscle is resected partially till fatty tissue of the ischiorectal fossa is visualized. ISR plus partial external sphincter resection is performed in those patients. The operative field in the pelvis is inspected for hemostasis and bleeding points are secured with fine silk ligatures or electrocautery.

Trans-anal approach

Patient position

The patient is placed in a more exaggerated lithotomy position with very elevated lower extremities to expose the anus and perineum. A moderate Trendelenburg position may facilitate perineal retraction. When a Lone Star retractor (Cooper-Surgical, Trumbull, CT) is placed around the anal verge, the lower edge of the tumor and anal anatomy are easily identified by using a flexible small spatula, and distance from the lower edge of the tumor to the dentate line or intersphincteric groove is finally measured (Fig. 6).

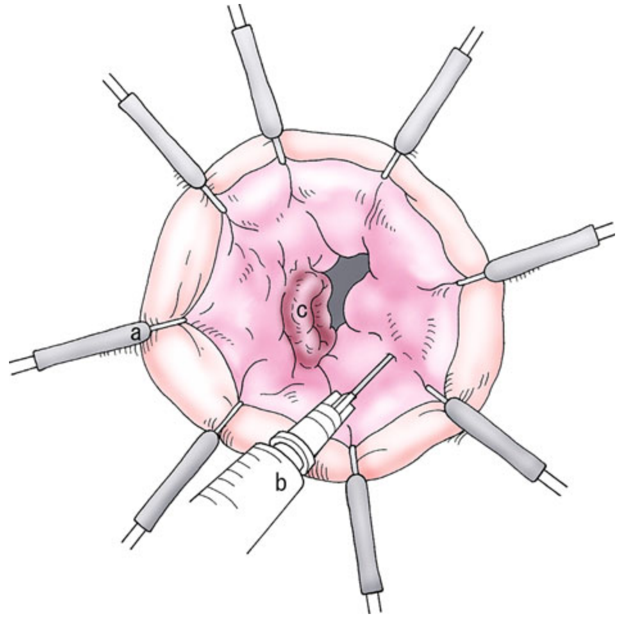

Fig. 6. Transanal approach; (**a**) Lone Star Retractor; (**b**) diluted epinephrine solution is infiltrated in the submucosa; (**c**) low rectal cancer

Diluted epinephrine solution is infiltrated in the submucosa circularly. The next step of perineal phase includes a circumferential incision of the mucosa, and the internal sphincter which is rather whitish, is subsequently incised, 1–2 cm distal to the tumor. Sometimes the internal sphincter is incised circumferentially but occasionally semi-circumferentially for a more limited lesion. Then the internal sphincter is carefully dissected from the external sphincter which is more reddish than the internal sphincter, in a bloodless plane. The anus is then closed transanally with about ten interrupted sutures or a purse-string suture and the anal stump is washed out with physiological saline and povidone-iodine to minimize the possibilities of tumor implantation and bacterial contamination. Following the irrigation, all contaminated instruments are discarded. It is desirable for the members of the surgical team to change gloves.

The dissection begins posteriorly and then laterally where the external sphincter is easier to identify and finishes anteriorly where the plane is more adherent. For tumors located 3 to 4 cm from the anal verge, dissection starts at the dentate line to remove the upper half of the internal sphincter. A partial ISR that disconnects anatomically the upper part of the internal sphincter from the puborectalis muscle is performed to obtain adequate distal margin in tumors close to the anal ring or above the anal canal. For tumors below 3 cm from the anal verge, dissection starts at the intersphincteric groove, removing the whole of the internal sphincter. The total ISR is necessary for tumors involving the internal sphincter. A distal margin of at least 1 cm is always necessary.

The second step of the perineal phase is a longitudinal dissection between the internal sphincter and striated sphincters. Threads of the closed anus are retracted upward, while the posterior portion of the external sphincter is pulled down and remaining attachments of the conjoined longitudinal muscle are divided. Once the intersphincteric space is entered, dissection continues upwards until it meets with the abdominal dissection plane. Transanal division of the superior sheath of the pelvic floor and of the presacral Waldeyer's fascia guided by the abdominal surgeon allows us to open the pelvic cavity posteriorly and it is understandable that the position of the anal canal in the pelvic diaphragm is surprisingly anterior (Fig. 7). The most difficult part of the dissection is anterior, where the plane is adherent due to intermingled fibers of the internal sphincter and the external sphincter. In the male, it is important not to proceed too deep, as it is possible to actually dissect deep to the lower edge of the prostate, putting the urethra at great risk. The upper end of bowel segment is grasped with a long Babcock forceps and delivered posteriorly through the anal canal. A small flexible spatula is introduced anteriorly to assist in exposure, while any remaining anterior attachments of the rectum are divided. Care should be taken to avoid unnecessary traction on the NVBs. Vessels that are not easily coagulated with electrocautery should be individually secured with interrupted suture. The location of both urethra and NVBs should be ascertained from time to time to avoid injury during the anterior dissection of the perineal phase.

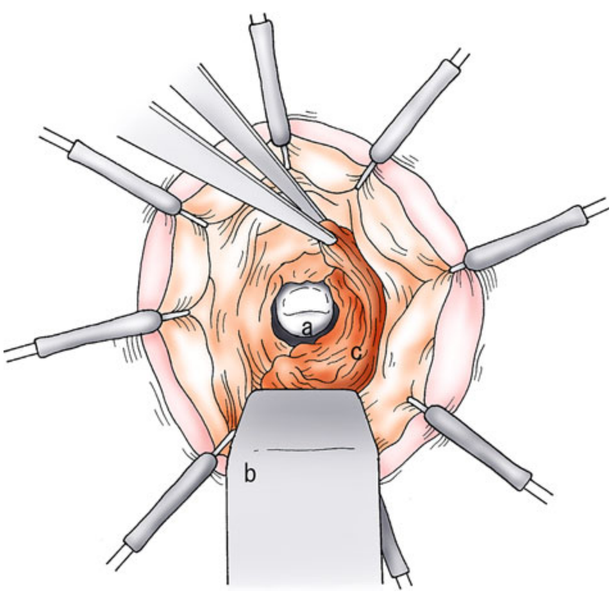

Fig. 7. Transanal division of Waldeyer's fascia under guidance by the abdominal surgeon; (**a**) finger guidance by abdominal surgeon; (**b**) small flexible spatula; (**c**) exposed external sphincter

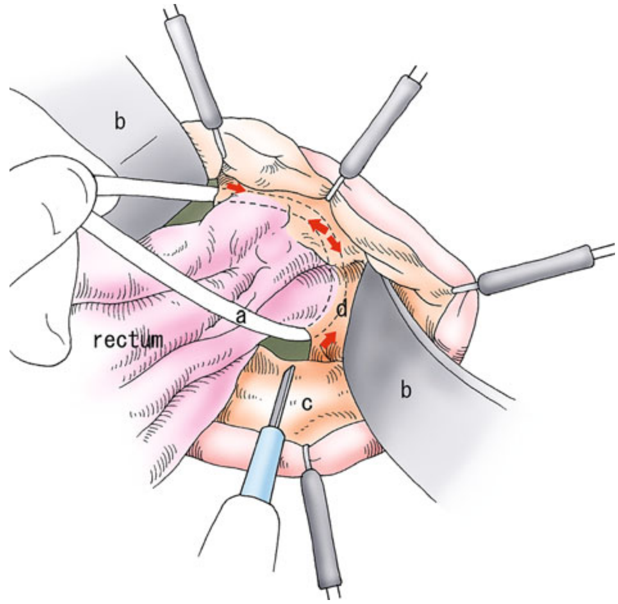

Fig. 8. Transanal anterior dissection by using a cotton tape; (**a**) a cotton tape around remaining muscle; (**b**) the small flexible spatula; (**c**) exposed external sphincter; (**d**) the anteriorly remaining muscle layer; (**e**) four red arrows indicate anterior dissection line

For tumors which cannot be pulled out transanally, a cotton tape is placed around the anteriorly remaining muscle layer from the perineum wound and any remaining anterior attachments of the rectum, including recto-urethralis muscle are divided using this cotton tape as a dissection indicator (Fig. 8). The rectum is then removed en bloc with the internal sphincter through the abdomen.

For patients treated with neoadjuvant treatment, the exact level of dissection of the internal sphincter, according to the distance from the anal verge is decided before radiation to avoid underestimation of the irradiated tumors and potential risk of tumor transsection [6].

Coloanal anastomosis

After removal of the specimen and irrigation of the pelvic cavity, the colonic stump for the anastomosis is pulled down and sutured to the remaining part of the anal canal. The stump of the colon must come up without angulation or tension by using a long Babcock forceps from the anus. The bowel is freed of all fatty attachments at the level of the future anastomosis. Obesity may make it impossible to perform the anal pouch anastomosis. If its color indicates an inadequate blood supply, the surgeon should not hesitate to remove a sufficient length until its viability is unquestionable. When adequate blood supply of the colonic stump is confirmed, four sutures at each quadrant of the anal canal, 1.5 cm from the stump should be placed to anchor the pulled down colon and to lessen possible tension on the anastomosis. Following this, the colonic stump is opened, while preventing gross contamination. Particular attention is given to initial four stitches with fine absorbable sutures to ensure accurate and secure approximation. These sutures include the full thickness of the colonic wall, as well as the remaining sphincter complex and anoderm. Several additional mattress sutures, totaling approximately twenty sutures may be placed to reinforce the anastomosis. Stitches are utilized for traction to secure adequate stitch interval. All stitches are finally cut together while rechecking each stitch interval. The patency of the anastomosis is tested by permission of thumb insertion. Finally, adequacy of the blood supply to the site of the anastomosis should be carefully inspected again. Instead of defunctioning stoma, the patient can be fed with total parenteral nutrition for seven to ten days after surgery. A defunctioning stoma should be considered if there is any suspicion regarding the technical imperfection of the anastomosis. Any peritoneal defect in the pelvis is closed with interrupted sutures. A drain may be inserted into the left side of the pelvis and brought out at the lower angle of the wound.

Pathological, functional and oncological outcomes

Morbidity

Postoperative early complications occurred in ranging 18% to 27% [5–8, 14], including anastomotic leakage, pelvic infection and abscess, colonic ischemia and necrosis, anovaginal fistula, bleeding. Late complication includes anastomotic stenosis, mucosal prolapse and bowel obstruction. The defunctioning stoma is closed, usually between 8 to 12 weeks.

Pathologic findings

All specimens are examined fresh in the operating theater for measurements of the tumor size and to determine macroscopic and microscopic resection margins. Radial and distal margins are considered positive if microscopic tumor is identified within 1 mm of resection [15].

In very low rectal cancers, the mesorectum is thin or absent at this level. Therefore, achieving negative radial margins is usually more challenging than obtaining distal clearance. In Weiser's study in only patients with locally advanced cancers, 93% of patients had radial margin >1 mm. This was comparable to those achieved by Schiessel (3% positive radial margin), Hohenberger (4%), Portier (4%), and Akasu (3%) [5, 8, 9, 12]. It must be noted, however, that these four studies included early stage tumors. In the series from Rullier analyzing 92 patients, most of whom had T3 disease, the radial margin was positive in 11% of cases [6].

Functional outcome

In terms of Pouch surgery, our group reported that a Jpouch was made in 24 patients, a transverse coloplasty pouch in 35, and a straight anastomosis in 47, according to the operator's preference [13]. Some fears were held for functional results after ISR procedures, because loss of the rectum and internal sphincter may induce anal dysfunctions, such as stool frequency, urgency, fragmentation, soiling, and fecal incontinence. Information on the potential functional adverse effects after total ISR should be provided to patients preoperatively.

In Rullier's study the functional results between patients with partial resection and those with subtotal resection of the internal sphincter were similar, despite a lower resting pressure in the latter group. Patients with a pouch anastomosis had better results than those with a straight anastomosis (67% vs. 37% with perfect continence).

These results suggest that performing a colonic J-pouch is more important than preservation of the internal anal sphincter in achieving good functional results after low coloanal anastomosis [6, 16].

Anal manometry demonstrated a significant reduction of mean resting pressure from 91.8 to 35 cm H_2O with no recovery after 2-years. Squeeze pressure showed only a transient decrease [5].

Recurrences and survival

In our series (108 patients), local recurrence and 5-year overall survival rates were 5.7% and 91%, respectively. Estimated cumulative local recurrence with T1–T2 tumors was significantly less than that with T3 tumors; 3-years rate of local recurrence, 0% versus 15%, respectively [13]. In a large series with 117 patients, Schiessel and associates reported a similar favorable local failure rate of 5.3% [10]. In another large series with 92 patients, Rullier and coworkers reported a better local recurrence rate (2%) and a slightly worse distant recurrence rate (19%), with a 5-year overall survival of 81% [6]. These differences were attributable to the background of their patients, 85% of whom had T3 or T4 tumors and 88% of whom received preoperative radiotherapy. For T3 tumors, our local recurrence rate of 14% without pre-operative radiotherapy is much higher than the 2% reported with radiotherapy, so adjuvant therapy should be considered for T3 tumors, as Rullier and coauthors recommended. But 86% of our patients with T3 tumors can achieve local control without radiotherapy. Therefore, it should be given only to high-risk patients, considering its toxicity to anal and sexual functions [13, 14]. The largest series of ISR comes from Japan. 103 patients had T3 tumors and 78 had T2 disease. R0 surgery was achieved in 225 of the 228 patients. During the median time of 41 months, the rate of local recurrence was 5.8% at three years and 5-year overall and disease-free survival rate were 91.9 and 83.3%, respectively [7]. Akasu reported results of multivariate analyses that with local recurrence after ISR, the resection margin, focal dedifferentiation and serum CA 19-9 level seem to be important. For distant recurrence, the lymph node status, histologic grade and tumor location need to be taken into account [14].

Conclusion

ISR can be an alternative to APR for selected rectal tumors situated at the anorectal junction, without compromising local control and chance of cure. It is likely that surgeon's experience and appropriate patients selection are the most important factors in achieving good oncological and functional results [6].

The techniques of ISR have modified the concept of sphincter-saving resection in the treatment of very low lying rectal cancer. ISR is suitable treatment for patients with extremely low rectal cancer of stage T1–T3 and well to moderately adenocarcinoma without distant metastases, provided that there is normal preoperative sphincter function.

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ISR practice and experience for extra-low rectal cancer in China

Zhenjun Wang and Jiagang Han

Epidemiology of rectal cancer in China: Including cancer incidence, distribution, etc.

Currently, the incidence of colorectal cancer in China is increasing year by year, with more than 170,000 new cases every year and the incidence rate ranking the fourth in cancer. In epidemiology, the colorectal cancer of Chinese has three characteristics compared with Western countries: (1) high incidence of rectal cancer, accounting for 65% of colorectal cancer, which is the most common malignant tumor of digestive tract; (2) high proportion of low rectal cancer, accounting for about 50% to 70% of rectal cancer; (3) high proportion of young people (<30 years old), about 15%. In major cities (Beijing, Shanghai, etc.), there was increased incidence of proximal colon cancer in recent years.

Current treatment of rectal cancer in China

From the current clinical practice, rectal cancer with the lower edge of cancer more than 2 cm from the dentate line, or more than 5 cm from the anal margin can usually be treated with TME (total mesorectal excision) to preserve the anal sphincter [1, 2]. However, for rectal cancer with the lower edge of cancer within 2 cm from the dentate line, or less than 5 cm from the anal margin, some surgeons fear that a tumour-free margin of 2 cm is not achievable, the potential of pelvic metastases and a postoperative malfunction of anus, so in theory they still use APR (abdominal perineal resection), with which patients have to bear the pain from anal removal and permanent colostomy. Permanent sigmoid colostomy causes inconvenience to the majority of patients, greatly affects their postoperative quality of life and thus leads to psychological problems in some patients. For this kind of low rectal cancer the important issue has to be resolved, how to guarantee the preservation of anal function without increasing local recurrence and other complications.

The safe distance for the distal cutting edge of rectal cancer was identified as to be 1–2 cm, which made the anal preservation of lower rectal cancer possible [3]. With the development of rectal cancer research, the distal infiltration distance of cancer gradually changed from the early 5 cm into 2 cm, the so-called golden rule. The result of large studies is that rectal cancer with distal infiltration of more than 1 cm is generally less than 3% [4]. In 2005, the American Society of Colorectal Surgeons recommended that in well-differentiated early rectal cancer, 1 cm of resection from the distal end can be considered safe [3]. Other investigators examined more than 200 cases of rectal cancer specimens of APR and found no infiltration and metastasis of subcutaneous sphincter and ischial rectal fossa, only 14% of late stage cases with infiltration into the outer sphincter and puborectalis muscle, indicating that the infiltration of full-thickness of sphincter is mainly seen in late stage cancer, while the direct or skip metastasis of ischial rectal fossa is very rare [5].

ISR specifications in China

ISR surgical techniques in China are as follows: (1) try to fully free the abdomen. If the patient is slim with lenient pelvis, the assistant should lift up anus with fist or sterile towels so as to get better exposure effects; usually freeing a certain distance toward the anal side between the outer sphincter ring and the intestinal wall also makes it easier to free the anal side. (2) directly excise through the full-thickness of the anal canal, perpendicular to it along the planned resection line, until the gap between inner and outer sphincter, and then free toward pelvis along the gap and join. When implementing resection through inner and outer sphincter, we must resolutely avoid the practice of stripping the rectal mucosa and vertically cut through the full-thickness of inner sphincter to reach the gap between inner and outer sphincter. (3) the surgeon should master the skills to identify inner and outer sphincter: the inner sphincter fibers are closely thin in pink white (which can be aptly called "sliced chicken"-like); in contrast, the outer sphincter fibers are thick in red (which can be aptly called "sliced beef"-like). The muscle bundles of both types are wrapped in sarcolemma, during which there is a natural gap. Finding the gap between the inner and outer sphincter is the key to success in accordance with the principles of radical surgery, and can also avoid bleeding during operation. (4) Parks and others believed there were no blood vessels at this level, but we found in the gap between inner and outer sphincter, usually there is a small artery respectively near clock 3 on the right side and near clock 10 on the left side of anal canal, which are branches of the anal canal artery; sometimes electric coagulation is not valid and ligation is needed, while for other blood vessels electric coagulation can be directly used. (5) Transverse colostomy or end ileostomy is suggested in the implementation of ISR, which on the one hand can be used to prevent the occurrence of anastomotic leakage, and on the other hand is conducive to the exercise and recovery of the patient's anal function after surgery. (6) If the patient is prepared for proximal colonic pouch or colon forming, be sure to calculate the length of intestine. The proximal intestine will be significantly reduced after completing the pouch or forming; if not planned well, it will lead to a great consistent tension or simply is not feasible. For individual patients with extremely narrow pelvis, the mesentery is relatively thick, so sometimes it cannot be dragged through the pelvic cavity after the colonic pouch is done, or will cause a blood circulation disorder when barely dragged, which needs to be considered in advance.

The proposal of modified partial ISR

In practice we found that most patients maintain a good anal function after ISR or partial ISR, but there are still defects in some patients with anal function.

To further improve anal function after low rectal cancer surgery, Wang et al. [6] reported on an ISR operation method in 2002 which retained part of the dentate line (modified partial ISR) (Fig. 1). After the anal surgery group fully revealed the tumor, cut open the full thickness of the anal canal perpendicular to its long axis in 1/2–1/4 quadrant of the lowest invasion of rectal cancer downward according to the diameter of primary tumor, 2 cm apart from the lower edge of the cancer. Then dissect upward along the anorectal ring, remove the dentate line on the cancer side, and join with the abdominal surgery group. On the tumour-free circumference cut off the rectum along the edge of the dentate line. During surgery the distal edge of the specimen was sent to quick frozen section for diagnosis and confirmed that no residual cancer in surgical margins. After resection of the specimen, it is optional to do colonic pouch at the distal end to join with the tumour side of the anal canal.

In clinical practice, the design of this method is based on that one side of rectal cancer usually has more invasions in the anal direction, so part of the dentate line can usually be kept on the opposite side of the tumour in order to preserve anal function. In recent years, we have mainly used this modified ISR method to retain part of the dentate line as much as possible, with the survival results similar to our own ISR surgical results, as well as to the postoperative recurrence rates and survival results reported in literature. In terms of anal function, the modified partial ISR which retains part of the dentate line has better effects than ISR which does not retain the dentate line.

Results of ISR study

From March 2000 to December 2009, 84 cases of ultra-low rectal cancer have been treated with ISR in the conventional open technique in our department. The distance between the lower edge of tumor and the dentate

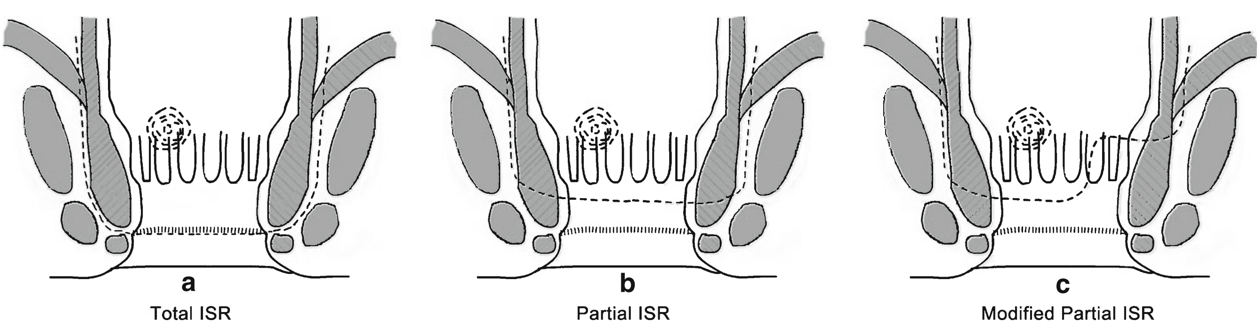

Fig. 1. Three options of ISR. (**a**) Total ISR involved complete excision of the internal sphincter. The cut line is at the intersphincteric groove. (**b**) Partial ISR involved partial excision of the internal sphincter. The cut line is between the dentate line and the intersphincteric groove. (**c**) Modified partial ISR: The cut line is below the dentate line at the tumour side. While at the opposite side of the tumour, the cut line was above the dentate line. ISR = intersphincteric resection [7]

line is less than 2 cm–5 cm in all cases, less than 2 cm in 38 cases, 4 cm in 1 case (firing failure of stapler) and 5 cm in 1 case (extremely narrow pelvis). As laparoscopic radical surgery for rectal cancer matured, we introduced the minimally invasive laparoscopic technology into ISR surgery, and made use of its minimally invasive advantages to carry out ISR for ultra-low rectal cancer. From November 2004 to December 2009, laparoscopic ISR has been implemented in 22 cases.

Patients underwent preoperative digital rectal examination, MRI or ultrasound endoscopy to determine the preoperative tumor staging of T1-T2. If the depth of tumor invasion is greater than T2 stage, after receiving neoadjuvant treatment (2 short courses of FOLFOX4 + 30 Gy radiotherapy), carry out MRI examination for re-staging of T1-T2 before dividing into groups.

All patients underwent radical ISR surgery, including 10 cases of total ISR, 24 cases of partial ISR and 72 cases of modified partial ISR. It was confirmed that the postoperative circumferential resection margin (CRM) is negative. According to the TNM classification system, postoperative histopathologic staging of open surgery group was 62 cases of Stage I, 6 cases of Stage II and 16 cases of Stage III; the postoperative staging of laparoscopic group was 17 cases of Stage I and 5 cases of Stage I. No perioperative death occurred.

ISR inclusion criteria

As ISR is implemented between the inner and outer sphincter, the technology should not be applied to Stage T3-T4 low rectal cancer with invasion of outer sphincter. For this category of patients, preoperative neoadjuvant radiotherapy and chemotherapy can be considered for tumor downstaging. If re-assessed as Stage T1-T2, ISR can be adopted; or inner and outer sphincter resection can be considered, i.e. to remove the invaded outer sphincter so as to retain the anus; also abdominal perineal resection can be considered.

For low rectal cancer with poor tumor differentiation, because the prognosis is poor, even if limited to T1-T2 tumor stage, the implementation of ISR should not be considered while adopting abdominal perineal resection or other surgical procedures.

As ISR removes rectum and part of inner sphincter, it is likely to affect anal function in patients after surgery, leading to increased frequency of defecation and bowel incontinence. If patients have poor preoperative anal function, their postoperative anal function may further deteriorate, therefore Wexner score and Kirwan grading should be used before surgery for detailed assessment of the anal function of patients. For those with poor preoperative anal function, especially elderly patients, we do not recommend the implementation of ISR surgery.

Therefore, we determined the inclusion criteria for accepting patients with ISR treatment: ① T1/T2 stage of ultra-low rectal cancer, anal cancer, or patients with extremely narrow pelvis (whether to receive neoadjuvant chemotherapy or not); ② tumor diameter greater than 1 cm and less than 5 cm; ③ well-differentiated tumor; ④ good anal function confirmed by preoperative examination; ⑤ no distant metastasis; ⑥ not with intestinal obstruction. The exclusion criteria are: ① tumor invasion of pelvic wall; ② tumor diameter greater than 5 cm; ③ poorly-differentiated tumor; ④ poor preoperative anal function.

ISR does not increase complications after surgery

Of 106 cases with ISR in our group, no perioperative death occurred. The main complications after surgery are as follows: 5 cases of wound infection (4.7%); 4 cases of patients who did not receive stoma had anastomotic leakage (3.8%); 6 cases of patients had anastomotic stenosis (5.7%); 1 case had presacral pelvic abscess 10 days after surgery (0.9%).

In this study, the most commonly seen complications after surgery are anastomotic leakage and anastomotic stenosis, which are significantly lower than the incidence of 4.5%∼13% of anastomotic leakage and 8.4%∼16% of anastomotic stenosis after ISR in domestic and foreign reports [8, 9], also lower than the incidence of 5%∼21% of anastomotic leakage and 6%∼10% of anastomotic stenosis after low anterior resection [10]. The main reasons for anastomotic leakage and anastomotic stenosis are anastomotic ischemia, local infection and preoperative pelvic radiotherapy. The implementation of TME technique in particular, makes the tissue around the rectum more completely removed. In our experience the lower anastomosis, the higher incidence of anastomotic stricture, which may be related to the exposure of surgical field, anastomotic tension and poor blood supply. The low incidence of postoperative complications in this study may be due to less use of preoperative radiotherapy and pelvic colonic pouch anastomosis, which fully guaranteed tension-free anastomosis. The low complication rate after surgery also showed that ISR can be safely used in the treatment of low rectal cancer.

ISR does not increase local recurrence rate

We regularly followed up our 104 patients after surgery (2 were lost), with an average follow-up of 62 months

(12~127 months). In the follow-up process, 2 cases of lung metastases occurred, accounting for 1.9% of the total number; 4 cases of pelvic local recurrence, accounting for 3.8% of the total.

Currently according to many studies abroad, the 5-year local recurrence rate after ISR is 2%~10.6% [5, 11, 12]. A study including meta-analysis of 612 cases of patients pointed out that, the postoperative local recurrence rate of ISR is 9.5%, indicating that ISR has similar results compared with traditional surgeries, such as low anterior resection and abdominoperineal resection [13]. The local recurrence rate of ISR we implemented is 3.8%, which is at a low level compared with the literature reports, so our ISR technology is mature and safe for low rectal cancer patients. Among the recurrence cases, 2 were total ISR, 1 was partial ISR, and 1 was modified partial ISR, indicating that different surgical techniques didn't significantly affect the local recurrence rate of patients after surgery, but also showing that the modified partial ISR proposed by Professor Wang Zhenjun did not increase local recurrence rate in patients, and can ensure radical treatment of tumor with the premise that we expect to improve the anal function in patients. But we should also be aware that, cutting open the rectum at the distal end of the tumor may lead to the implantation of tumor cells into the pelvic cavity, and therefore after cutting the anorectal mucosa and subcutaneous tissue, the anal canal should be closed with a suture. Meanwhile we do also a lot of washing after removing the specimen. These measures may help to reduce the local recurrence rate.

ISR does not reduce survival rate

We regularly followed up our 104 patients after surgery (2 were lost), with an average follow-up of 62 months (12–127 months). In the follow-up process, 6 patients died, 4 of which were due to recurrence and distant metastasis after tumor surgery, 1 died of cerebral hemorrhage 7 years after surgery, and 1 died of myocardial infarction 5 years after surgery. After surgery, the 5-year overall tumor-related survival rate was 96% while the tumor-free survival rate was 91.6% (Fig. 2).

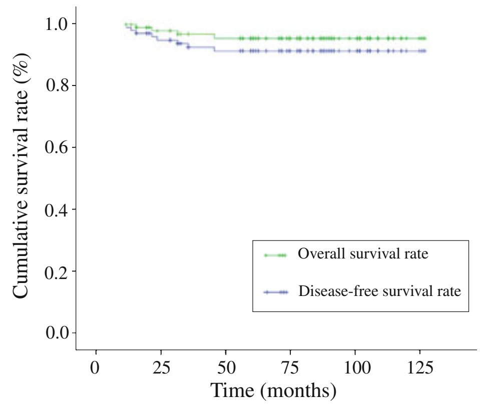

Fig. 2. Kaplan-Meier Survival Curve shows the overall survival rate and disease-free survival rate after ISR

Saito et al. [5] reported 228 patients with rectal cancer located < 5 cm from the anal verge who underwent ISR at seven institutions. During the observation, five-year overall and disease-free survival rates were 91.9 percent and 83.2 percent. Recently, Chamlou et al. [11] found a 82 percent and 75 percent rate of five-year overall and disease-free survival in 90 patients respectively. In our study, the 5-year overall survival rate was as high as 95.6% and the disease-free survival rate was 91.6%; in the 4 cases of death, 3 were stage III patients, 1 was stage II patient, whereas the survival rate of stage I patients was 100%, which may be related to the standard TME technology and strict inclusion criteria we adopted, especially to the T1/T2 tumor-based cases. The above results show that the ISR series of surgery do not reduce the survival rate of low rectal cancer patients after surgery, which helps to retain the anus, improve the quality of life of patients while ensuring radical treatment of tumor and survival of patients.

ISR has a better postoperative anal function

We underwent evaluation of anal function based on Kirwan grading on 101 patients 12 months after surgery, with the results shown in Table 1, of which the rate of patients receiving total ISR with a good anal function

Table 1: Comparison of Kirwan grading with three types of ISR 12 months after surgery in the open surgery group

($n = 101$)			
Kirwan grading	Modified partial ISR ($n = 70$)	Partial ISR ($n = 22$)	Total ISR ($n = 9$)
I (normal) (%)	47 (67)	9 (41)	–
II (incontinence of gas) (%)	20 (29)	8 (36)	3 (33)
III (occasional mild overflow) (%)	3 (4)	5 (23)	5 (56)
IV (underwear often contaminated) (%)	–	–	1 (11)
V (stoma required) (%)	–	–	–

$P = 0.011$, modified partial ISR *vs.* partial ISR; $P = 0.000$, modified partial ISR *vs.* total ISR; $P = 0.035$, partial ISR *vs.* total ISR.

was 33% (Kirwan I and II), partial ISR was 77%, while modified partial ISR was 96%. The anal function of patients with modified partial ISR was superior to those with partial ISR ($P = 0.011 < 0.017$) and total ISR (Kirwan grading, $P = 0.000 < 0.017$) (Table 1). None of the patients in each group received stoma because of poor bowel control after surgery.

Fecal incontinence after ISR is primarily caused by anal-sphincter insufficiency. Physiologic studies demonstrated significant decrease in resting pressure after the removal of the internal sphincter [14, 15]. The advent of sphincter-saving surgery and restorative proctocolectomy has emphasized the major contribution of the internal anal sphincter to prevent fecal leakage [16]. Therefore, we proposed modified partial ISR to retain part of the dentate line on the opposite side of tumor. Literature reported that the rate of good anal function after surgery was 29%–86.3%, patients with stoma due to poor bowel function were about 0–0.8% [11, 17]. In our study, the rate of good anal function 12 months after modified partial ISR was 96%, which is significantly higher than partial ISR of 77% and total ISR of 33%, confirming the modified ISR which retains part of sphincter and dentate line helps patients improve and enhance their anal functionality. Therefore, in order to reduce the incidence of anal incontinence after ISR, we recommend retaining the sphincter and the dentate line as much as possible with the premise of ensuring radical treatment.

The advantages of laparoscopic ISR

In clinical work, we found that with the increase of cases and the constant improvement of technology, laparoscopic surgery has many advantages for the treatment of ultra-low rectal cancer with anal sphincter preservation. Laparoscopy can go deep into the pelvic cavity and show the local anatomy from various angles, so that physicians can perform detailed anatomy of the lower rectum to its muscle under direct vision, free the rectum toward the distal end as much as possible to reach the level of puborectalis muscle. Under laparoscopy we freed the rectum as much as possible to the dentate line level, and then physicians of the perineal group removed specimens through perineal approach and placed the proximal end of bowel into pelvic cavity. After the laparoscopic examination of intestinal location, physicians of the perineal group interruptedly joined the colon – anal canal anastomosis with a suture through the anus. This treatment not only ensures the scope of surgical resection, but can also reduce surgical risks and the difficulty of the operation.

Our study confirmed that to implement ISR by using laparoscopic surgical techniques has a clear vision of operation, relatively minor trauma, slight physical interference, an early recovery of normal activities after surgery and other advantages, which does not increase local recurrence rate or lower survival rate. We believe that with technological development and update of surgical instruments, this technique will gradually mature and benefit more and more patients.

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Intersphincteric resection of low rectal tumors: Experience from a German Cancer Center

Jonas Göhl, Werner Hohenberger, and Susanne Merkel

Summary

Intersphincteric abdomino-peranal resection is the very last option for sphincter preservation of tumors of the lower third which otherwise would not be resectable with preservation of the sphincter by an abdominal approach alone.

We analyzed the data of 725 patients with a carcinoma of the lower third of the rectum who underwent primary treatment for stage I–III disease by low anterior resection, abdomino-peranal (intersphincteric) resection or abdominoperineal excision between 1985 and 2007. Three time periods from 1985–1994, 1995–2001 and 2002–2007 were compared.

The rate of intersphincteric resection increased from the first to the second period from 3% to 27% and finally decreased since 2002 to 18%. The rate of abdominoperineal excision continuously decreased from the first to the last time period from 56% to 28%.

The rate of postoperative complications was not increased in intersphincteric resections with 25.6% in the last time interval and no postoperative death was observed after intersphincteric resection. The overall 5-year rate of locoregional recurrence decreased from 18% to 5.4% from the first to the last time period. In patients with intersphincteric resection this rate was 22.7% in the prior two periods when most patients were treated by surgery alone, while in the last period with routine use of preoperative radiochemotherapy no patient developed a locoregional recurrence. The cancer-related 5-year survival rate was not altered by intersphincteric resection.

In carcinomas of the lower third of the rectum, the procedure of abdomino-peranal intersphincteric resection can reduce the need for rectal excision with a permanent stoma by 20%. Neoadjuvant radiochemotherapy must be recommended to reduce locoregional recurrence to an acceptable level.

Introduction

R0 resection, preservation of the sphincter muscle and avoidance of local recurrence are currently considered to be the foremost target criteria in the treatment of rectal cancer. All these parameters can be positively influenced by neo-/adjuvant radio(chemo)therapy [1–5].

Additionally efforts have been made in recent years to increase the rate of sphincter preservation by surgical technique, meaning by ultra-low resections. The most extended form of rectal resection representing the very last option for preservation of the sphincter is the intersphincteric abdomino-peranal resection for tumors of the lower third which otherwise would be treated by abdominoperineal excision [6–11].

In this report we describe the process of implementing intersphincteric resection with a constant quality control and monitoring in the routine treatment of low rectal carcinoma. We analyzed our patient collective from 1985 to 2007 in three time intervals with cutoff points in 1995 and 2002. In our cancer center, intersphincteric resection is a standardized procedure since 1995. Since 2002 the indication is restricted to T1 and T2 tumors in the intersphincteric level without infiltration of the puborectal sling and all patients are consistently treated with preoperative radiochemotherapy.

Patients and methods

Patients

Our analysis is based on the prospectively collected data from the Erlangen registry of colorectal carcinomas (ERCRC). All patients undergoing primary treatment for invasive colorectal cancer at the Department of Surgery, University Hospital Erlangen, Germany, are registered without selection. General epidemiological data, clinical findings, treatment, histopathological findings and follow-up are documented using a standardized system based on the international documentation system of colorectal carcinoma [12–14]. Histopathological findings including residual tumor classification were classified according to the UICC TNM classification (7th Edition 2009 [14]). The distance of the tumor from the distal resection line was measured in mm, tension-free, in the fresh specimen, also the circumferential margin distance to the mesorectal fascia. Postoperative complications were defined as all events with a need for diagnostic or therapeutic procedures, or a prolongation of the hospital stay. Postoperative mortality includes all patients who died postoperatively in hospital without regarding the time interval from the operative procedure (hospital mortality).

Here we analyze the data of 725 patients with a primary invasive carcinoma located in the lower third of the rectum (7.5 cm or less from the anal verge as measured with a rigid rectoscope) with surgical resection between 1985 and 2007. Only patients without distant metastases who had surgical treatment confined to low anterior resection, abdomino-peranal (intersphincteric) resection or abdominoperineal excision were included. Each procedure included total mesorectal excision as a standardized regional lymph node dissection to the origin of the inferior mesenteric artery. Patients with other previous or synchronous malignant tumors were excluded from the analysis as were carcinomas arising from familial adenomatous polyposis (FAP), ulcerative colitis or Crohn‘s disease.

Patients were followed for a total of 5 years, during the first two years every 6 months, thereafter every 12 months corresponding to the recommendations of the German Cancer Society. After completion of regular follow-up, patients or their family doctors were contacted by phone or mail at longer intervals. The median follow-up time was 80 months (range: 0–25 years).

Table 1: Patients ($n = 725$)

	1985–2007	1985–1994	*p*	1995–2001	*p*	2002–2007
n (%)	725	303 (41.8%)		205 (28.3%)		217 829:959
Sex			0.035		0.561	
Male	487 (67.2%)	190 (62.7%)		147 (71.7%)		150 (69.1%)
Female	238 (32.8%)	113 (37.3%)		58 (28.3%)		67 (30.9%)
Age (years)			0.499		0.660	
Median (range)	62 (21–92)	61 (21–85)		61 (27–92)		62 (22–87)
Operative procedure			<0.001		<0.001	
LAR	275 (37.9%)	100 (33.0%)		58 (28.3%)		117 (53.9%)
Intersphincteric res.	104 (14.3%)	10 (3.3%)		55 (26.8%)		39 (18.0%)
APE	346 (47.7%)	193 (63.7%)		92 (44.9%)		61 (28.1%)
Pouch			<0.001		<0.001	
No	471 (65.0%)	303 (100%)		157 (76.6%)		125 (57.6%)
Yes	254 (35.0%)	0		48 (23.4%)		92 (42.4%)
Radiochemotherapy			<0.001		<0.001	
None	388 (53.5%)	271 (89.4%)		81 (39.5%)		36 (16.6%)
Neoadjuvant	253 (34.9%)	10 (3.3%)		80 (39.0%)		163 (75.1%)
Adjuvant	84 (11.6%)	22 (7.3%)		44 (21.5%)		18 (8.3%)
R-classification			0.075		0.504	
R0	688 (94.9%)	290 (95.7%)		198 (96.6%)		210 (96.8%)
R1	16 (2.2%)	4 (1.3%)		7 (3.4%)		5 (2.3%)
R2	9 (1.2%)	8 (2.6%)				1 (0.5%)
RX	2 (0.3%)	1 (0.3%)				1 (0.5%)
Stage			<0.001		<0.001	
Stage I	161 (22.2%)	77 (25.4%)		49 (23.9%)		35 (16.1%)
Stage II	115 (15.9%)	78 (25.7%)		31 (15.1%)		6 (2.8%)
Stage III	195 (26.9%)	137 (45.2%)		45 (22.0%)		13 (6.0%)
Stage y0	38 (5.2%)	0		8 (3.9%)		30 (13.8%)
Stage yI	83 (11.4%)	3 (1.0%)		22 (10.7%)		58 (26.7%)
Stage yII	64 (8.8%)	3 (1.0%)		22 (10.7%)		39 (18.0%)
Stage yIII	69 (9.5%)	5 (1.7%)		28 (13.7%)		36 (16.6%)

LAR low anterior resection; *APE* abdomino-perineal excision.

The analysis compares parameters for the periods 1985–1994, 1995–2001 and 2002–2007. In 1995, based on the therapeutic algorithm, we started to evaluate the indication for an abdomino-intersphincteric-peranal approach in patients with tumors of the lower rectum prospectively. Patients', tumor and treatment characteristics are shown in Table 1.

Locoregional recurrence was defined as the presence of any anastomotic, pelvic or perineal tumor documented by clinical and/or pathological examination even if distant metastases were present. Both symptomatic and asymptomatic locoregional recurrences were recorded.

For the analysis of cancer-related survival and locoregional recurrence rates the following patients were excluded: 27 (3.7%) patients undergoing noncurative resection (R1, R2), 25 (3.6%) patients who died postoperatively and 9 (1.2%) patients with unknown tumor status at the end of the patient evaluation (1 January 2011) as lost to follow-up.

Cancer-related survival and locoregional recurrence rates were calculated using the Kaplan-Meier method. In the analysis of cancer-related survival cancer-related death was defined as event, i.e. death with recurrent locoregional carcinoma and/or distant metastases, while patients who died without evidence of disease were censored. In the analysis of locoregional recurrence an event was defined at the point of diagnosis of locoregional recurrence and the survival time of all patients who remained free of locoregional recurrence was censored. The 95% confidence intervals (95% CI) were calculated in accordance with Greenwood. For comparison of survival the logrank test was used.

The χ^2 and Fisher's exact test were used to compare frequencies. A p-value ≤ 0.05 was considered significant. All analyses were carried out with the IBM SPSS Statistic 19.0 software package.

Patient selection for abdomino-peranal intersphincteric resection

In all patients, the evaluation of the localization and extent of the primary tumor was based on a digital rectal examination, rigid rectoscopy, CT scan or MRI of the pelvis. In addition, in patients without obstruction endosonography was performed whenever possible.

Since 1995 the algorithm of patient selection was established by two experienced senior surgeons to evaluate the indication for an abdomino-peranal approach in cases presenting with tumors of the lower rectum.

Inclusion criteria:

- A minimum distance from the lower edge of the tumor to the dentate line 0.5 cm in preoperative rectoscopy;
- Carcinomas confined to the rectal wall (uT1 or uT2) without infiltration of the puborectal sling on ultrasonography;
- Tumors with invasion beyond the outer border of the muscularis propria only when located above the puborectal sling (patients with infiltration of the external anal sphincter were suggested as contraindication for intersphincteric resection);
- Low grade tumors (G1 or G2) in preoperative biopsy;
- Preoperative sufficient sphincter function;
- Patients eligible for neoadjuvant radiochemotherapy. This was required for all patients since 2002.

Exclusion criteria:

Patients with obviously impaired sphincter function and signs of incontinence (documented by sphincter manometry or clinical findings) were not accepted for intersphincteric resection.

Technique of abdomino-peranal intersphincteric resection

The majority of patients with low rectal cancer can be resected by an abdominal approach, only. However, even then an intersphincteric dissection is used. In these patients it is mandatory to divide the paired coccygeo-rectal muscles which originate from the coccygis joining the lowest part of the rectum posteriorly below the mesorectal fascia. Their presentation may differ relevantly; sometimes they are thin like a strain-like ligament; more frequently, they are to be identified as a muscular structure, sometimes reaching a diameter up to 3 or 4 mm

Especially in the case of elderly women with large excavation of the pelvic floor muscles and a wide pelvis, tumors with the above-mentioned criteria can often be removed by an (ultra)-low anterior rectal resection carried out exclusively by abdominal approach via intersphincteric dissection. These patients are not included into this patient collective. In male patients with a narrow pelvis, obesity and firm pelvic floor muscles, an abdominal approach is usually not possible, even when oncological considerations which are described above would allow preserving the anal sphincter. Furthermore, if the intended dissection line cannot be assessed from an abdominal approach or direct vision during dissection in the lower third of the rectum close to the pelvic floor without the risk to cut through the tumor the indication for abdomino-peranal intersphincteric resection is justified. For this purpose, the anal canal is exposed with the aid of rubber retractors (Lone Star Retractor System^{TM}) hooked into the intermediate zone in circular fashion. In this manner, the lower edge of the tumor can always be visualized. In

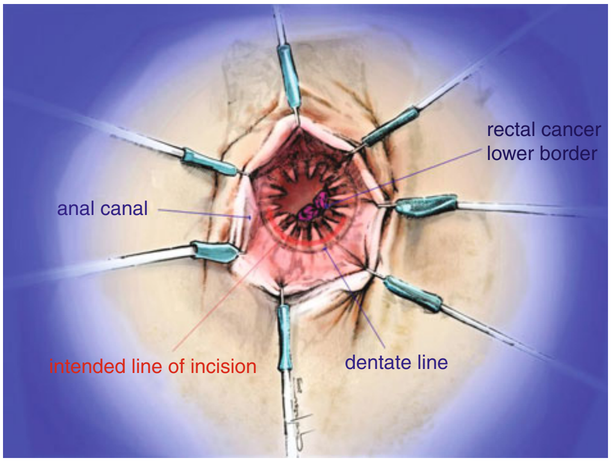

Fig. 1. Incision line for the peranal part of the intersphincteric resection of lower third rectal carcinoma close to the dentate line

the region of the dentate line, below the lower edge of the tumor a circular incision is made with the electric scalpel. Beginning dorsally, the internal sphincter is completely divided (Fig. 1). When the correct intersphincteric plane has been reached a spontaneous retraction of the rectal wall cranialwards can be observed. This is not possible anteriorly due to intermuscular connections. After preoperative irradiation, this phenomenon can also be missed. For this reason, starting dorsally, the internal anal sphincter is divided stepwise in circular fashion and the dissection is then continued in the intersphincteric plane, cranial to the upper edge of the external sphincter (puborectal sling). The distance involved differs from individual patient criteria, usually being longer in men than in women, mostly 3 to 5 cm. In the anterior quarter of the circumference, sharp dissection is needed, because of connective tissue between the internal sphincter and the external sphincter. In particular in anterior tumors, the plane of the dissection must be strictly followed in order not to expose or cut the tumor which would worsen oncologic prognosis.

If the rectum is completely mobilized from the anterior approach down to the pelvic floor, the puborectal sling is exposed and, if technically possible, the intersphincteric space is opened, the dentate line of the anal canal is divided and the intersphincteric dissection is continued for a maximum of 2 to 4 cm, then the resection is completed from the peranal approach.

Following the intersphincteric preparation, the descending colon is divided proximally at the level of the transition of the descending to the sigmoid colon.

A frozen-section examination of the resected material is carried out to ensure the oncologically relevant criteria (grading, R classification). If the tumor is removed in healthy tissue (negative distal and circumferential margin) with a distal margin of clearance of at least 0.5 cm, the intersphincteric resection is considered to be oncologically adequate.

For the anastomosis, the colon or a prepared pouch is drawn preanalwards through the puborectal sling and anastomosized end-to-end or, in the case of a J-pouch side-to-end, using single sutures. At the colon, the anastomosis is done extramucosally and in the anal canal it includes its full-thickness or any persisting parts of the lower internal sphincter muscle.

In obese patients, the presence of fat makes the colonic pouch voluminous and therefore, it may be impossible to draw it through the puborectal sling for anastomosis in the anal canal. In such cases, a straight colo-anal anastomosis is preferred. In all patients with a peranally sutured anastomosis a deviation with a protective loop ileostomy is felt to be essential.

Since 1995, in all patients receiving an anteriorly constructed anastomosis, the distance of the latter from the dentate line has been measured intraoperatively using the rigid rectoscope. The median of this distance was 10 mm (0–20 mm). In all intersphincteric operations, the anastomosis was within the region of the dentate line (intermediate zone) or below.

Results

Neoadjuvant or adjuvant radiochemotherapy

In the first period between 1985 and 1994, 90% of the patients did not receive radiochemotherapy. Only 3% had neoadjuvant and 7% had adjuvant radiochemotherapy. In the second time period between 1995 and 2001, the percentage of patients receiving radiochemotherapy increased significantly to 60%, 39% preoperatively and 22% postoperatively. Patients undergoing an abdominoperineal excision or intersphincteric resection received such treatment more often, in 66% and 65%, respectively, as compared to patients with low anterior resection (47%, $p = 0.135$). Since 2002, all patients who were planned for intersphincteric resections in malignant disease were intended to be treated by neoadjuvant radiochemotherapy. Only two patients had intersphincteric resections without preoperative radiochemotherapy. In these patients preoperatively diagnosed adenomas were proven to be carcinomas in the histopathological findings postoperatively.

Operative procedures

The rate of abdominoperineal excisions decreased significantly over the three time intervals from 63.7% to 28.1%, while the rate of intersphincteric resections increased between 1995 and 2001 (26.8%) and finally decreased in the period from 2002 until 2007 to 18.0%. The percentage of low anterior resections remained relatively constant at 33% and 28% until 2001 and increased to 53.9% in the last period (Table 1). The increase of low anterior resections and decrease of abdominoperineal excisions between the periods were statistically significant ($p < 0.001$).

Distal margin of clearance

Comparing the distal margin of clearance between low anterior resections and intersphincteric resections we did not found a significant difference ($p = 0.183$). The median measurement of the margin revealed median 20 mm in low anterior resections (20 mm, 18.5 mm and 18 mm within the three time periods) and median 15 mm in intersphincteric resections (15 mm, 20 mm, 12.5 mm within the three time periods).

Circumferential margin

In 59 of 104 intersphincteric resected specimens circumferential resection margin (CRM) was documented. While in 56 patients CRM was negative (distance of the tumor to circumferential margin >1 mm), it was

Table 2: Operative procedure and stage distribution

	All	LAR	*p*	Intersphincteric resection	*p*	APE
1985–2007	725	275 (37.8%)		104 (14.3%)		346 (47.7%)
Stage			0.005		<0.001	
Stage I		75 (27.3%)		20 (19.2%)		66 (19.1%)
Stage II		34 (12.4%)		9 (8.7%)		72 (20.8%)
Stage III		71 (25.8%)		16 (15.4%)		108 (31.2%)
Stage y0		17 (6.2%)		12 (11.5%)		9 (2.6%)
Stage yI		32 (11.6%)		24 (23.1%)		27 (7.8%)
Stage yII		19 (6.9%)		12 (11.5%)		33 (9.5%)
Stage yIII		27 (9.8%)		11 (10.6%)		31 (9.0%)
1985–1994	303	100 (33.0%)		10 (3.3%)		193 (63.7%)
Stage			0.328		0.652	
Stage I		24 (24%)		5 (50%)		48 (24.9%)
Stage II		20 (20%)		2 (20%)		56 (29.0%)
Stage III		53 (53%)		3 (30%)		81 (42.0%)
Stage y0		0		0		0
Stage yI		0		0		3 (1.6%)
Stage yII		0		0		3 (1.6%)
Stage yIII		3 (3%)		0		2 (1.0%)
1995–2001	205	58 (28.3%)		55 (26.8%)		92 (44.9%)
Stage			0.661		0.295	
Stage I		22 (38%)		14 (26%)		13 (14%)
Stage II		10 (17%)		7 (13%)		14 (15%)
Stage III		9 (16%)		12 (22%)		24 (26%)
Stage y0		3 (5%)		3 (6%)		2 (2%)
Stage yI		4 (7%)		8 (15%)		10 (11%)
Stage yII		5 (9%)		5 (9%)		12 (13%)
Stage yIII		5 (9%)		6 (11%)		17 (19%)
2002–2007	217	117 (53.9%)		39 (18.0%)		61 (28.1%)
Stage			0.011		0.153	
Stage I		29 (24.8%)		1 (3%)		5 (8%)
Stage II		4 (3.4%)		0		2 (3%)
Stage III		9 (7.7%)		1 (3%)		3 (5%)
Stage y0		14 (12.0%)		9 (23%)		7 (12%)
Stage yI		28 (23.9%)		16 (41%)		14 (23%)
Stage yII		14 (12.0%)		7 (18%)		18 (30%)
Stage yIII		19 (16.2%)		5 (13%)		12 (20%)

LAR low anterior resection; *APE* abdomino-perineal excision.

positive (≤1 mm) in 3 patients (5%; 1985–2007). In the last period (2002–2007) the rate of CRM+ was 3% (1/30). In low anterior resections, CRM was positive in 3% (6/197; 1985–2007) and 2% (2/101; 2002–2007), while it was 27% (28/105; 1985–2007) and 11% (5/45; 2002–2007) in patients who had abdominoperineal excisions.

R0 resections

The rate of R0 resection was already high in the first time period with 95.7% and increased non-significantly to 96.8% in the last period while the R2 resection rate decreased from 2.6% to 0.5%.

Stage distribution

The prognostic favorable UICC stages y0 and yI increased from 1% to 40.5% during the three periods due to the more frequently use of neoadjuvant radiochemotherapy. In the last period the percentage of ypT0 und ypT1 tumors in intersphincteric resections was 64% (Table 2). Histologically proven complete remissions following neoadjuvant radiochemotherapy (stage y0) increased from the second to the third period from 3.9% to 13.8%.

The rate of stage III patients without preoperative radiochemotherapy decreased from 45.2% in the first period to 22.0% in the second and to 6% in the last period. In contrast stage yIII after preoperative radiochemotherapy only increased from 1.7% over 13.7% to 16.6% ($p < 0.001$; Table 2).

Postoperative complications and mortality rates

Over the whole period, the rate of postoperative complications after low anterior resection and intersphincteric resection was 25.5% and 25.0%, respectively. This rate was significantly higher after abdominoperineal excision with 39.6% ($p = 0.007$). Also postoperative mortality was lower after low anterior resection and intersphincteric resection with overall rates of 2.5% and 1.9%, respectively, while it was 4.3% after abdominoperineal excision.

Focusing on the three time intervals, the postoperative complication rate decreased in low anterior resections from 30.0% to 17.9%, in intersphincteric resections from 30% to 25.6%, and increased in abdominoperineal excisions from 35% to 42%. While there was no postoperative death after low anterior resections and intersphincteric resections in the last time interval, the mortality rate was 3.3% after abdominoperineal excision (Table 3).

Locoregional recurrences

The 5-year local recurrence rate decreased during the three periods from 18.7% over 14.4% to 5.4% in the last period (Table 4). Within the last period, the local recurrence rate was 5.6% after anterior resection and 9.2% after abdominoperineal excision. None of the 39 patients treated by intersphincteric resection in the last period developed a locoregional recurrence.

It is questionable to compare the different stages in a mixed cohort treated by primary surgery and as well treated by neoadjuvant radiochemotherapy followed by surgery. A prognostic favourable group was identified in patients with stage I, y0 and yI. In these patients we found

Table 3: Operative procedure and postoperative complications/mortality

	LAR	*p*	Intersphincteric resection	*p*	APE
1985–2007	275		104		346
Postoperative complications	70/275 (25.5%)	0.928	26/104 (25.0%)	0.007	137/346 (39.6%)
Postoperative mortality	7/275 (2.5%)	0.723	2/104 (1.9%)	0.258	15/346 (4.3%)
1985–1994	100		10		193
Postoperative complications	30/100 (30.0%)	1.0	3/10 (30%)	1.0	68/193 (35.2%)
Postoperative mortality	5/100 (5.0%)	0.443	1/10 (10%)	0.435	10/193 (5.2%)
1995–2001	58		55		92
Postoperative complications	19/58 (32.8%)	0.304	13/55 (23.6%)	0.005	43/92 (46.7%)
Postoperative mortality	2/58 (3.4%)	1.0	1/55 (1.8%)	1.0	3/92 (3.3%)
2002–2007	117		39		61
Postoperative complications	21/117 (17.9%)	0.297	10/39 (25.6%)	0.084	26/61 (42.6%)
Postoperative mortality	0		0	0.253	2/61 (3.3%)

LAR low anterior resection; *APE* abdomino-perineal excision.

Table 4: Locoregional recurrence (LR) in the lower third of the rectum after R0 resection, postoperative mortality excluded, $n = 664$

	n	5-Y-LR (95% CI)	p
1985–2007	664	13.4 (10.7–16.1)	
Operative procedure			
LAR	265	11.4 (7.5–15.3)	
Intersphincteric resection	98	12.2 (5.5–18.9)	0.770
APE	301	15.5 (11.2–19.8)	0.168
1985–1994	270	18.7 (13.8–23.6)	
Operative procedure			
LAR	95	20.0 (11.4–28.6)	
Intersphincteric resection	7	0	0.261
APE	168	18.5 (12.4–24.6)	0.271
1995–2001	189	14.4 (9.1–19.7)	
Operative procedure			
LAR	55	9.2 (5.8–16.8)	
Intersphincteric resection	53	21.6 (4.1–33.0)	0.154
APE	81	13.1 (5.1–21.1)	0.393
2002–2007	205	5.4 (2.1–8.7)	
Operative procedure			
LAR	115	5.6 (1.3–9.9)	
Intersphincteric resection	38	0	0.154
APE	52	9.2 (0.4–18.0)	0.067

LAR low anterior resection; *APE* abdomino-perineal excision.

Table 5: Cancer-related survival rates in the lower third after R0 resection, postoperative mortality excluded, $n = 664$

	n	5-Y-SR (95% CI)	p
1985–2007	664	81.8 (78.7–84.9)	
Operative procedure			
LAR	265	85.8 (81.5–90.1)	
Intersphincteric resection	98	89.3 (83.0–95.6)	0.607
APE	301	76.0 (70.9–81.1)	0.006
1985–1994	270	75.5 (70.2–80.8)	
Operative procedure			
LAR	95	77.3 (68.5–86.1)	
Intersphincteric resection	7	66.7 (29.1–100)	0.343
APE	168	74.7 (68.0–81.4)	0.603
1995–2001	189	85.4 (80.1–90.7)	
Operative procedure			
LAR	55	90.9 (83.3–98.5)	
Intersphincteric resection	53	86.4 (77.0–95.8)	0.261
APE	81	80.5 (71.3–89.7)	0.579
2002–2007	205	87.2 (82.3–92.1)	
Operative procedure			
LAR	115	90.1 (84.2–96.0)	
Intersphincteric resection	38	97.2 (91.9–100)	0.137
APE	52	73.0 (59.7–86.3)	0.005

LAR low anterior resection; *APE* abdomino-perineal excision.

a 5-year locoregional recurrence rate of 5.8% (95% CI 2.9–8.7) for all periods (1984–2007) and 1.8% (95% CI 0.2–3.4) for the third period from 2002–2007. In patients with stage II, yII, III and yIII the locoregional recurrence rates were significantly higher, 19.3% (15.4–23.4) for 1984–2007 and 12.5% (4.7–20.3) for the last period 2002–2007 ($p < 0.001$ and $p = 0.001$, respectively).

Cancer-related survival rates

The cancer-related 5-year survival rate after R0 resection in stage I–III disease after exclusion of patients who died postoperatively increased from 57.5% in the first period over 85.4% in the second period to 87.2% in the last period. Since 1995 5-year survival rates are stable after low anterior resection with about 90% and increased after intersphincteric resections from 86% to 97% while a decrease of the survival rate was observed in patients with abdominoperineal excision from 81% to 75% (Table 5).

Conclusion

In the literature, the term "intersphincteric resection" is increasingly used. However, in our common practice, intersphincteric preparation is almost always part of the procedure of routine low anterior resection with total mesorectal excision. This does not even differ from another "upcoding" terminology using the term "ultralow" resection. For this reason and to make the difference clear that the patients involved needed an peranal transsection of the dentate line or less frequently of the most distal part of the rectal wall, we introduced the term "abdomino-peranal intersphincteric resection" [15].

Finally, beginning at the end of the 1980s, the method of intersphincteric abdomino-peranal resection was introduced in our hospital. Since 1995 standardization was implemented using a therapeutic algorithm to prospectively select patients for this operative procedure. Patients with pre-existing continence problems were excluded. In this way, the extirpation rate for cancer of the lower third of the rectum could be reduced from 64% to 45%. In the literature, the reported extirpation rates for carcinomas at this site vary between 20% and 55% [16–18]. With gaining experience, we have learned that a strict patient selection due to the tumor spread and characteristics is indispensable with special regard to the circumferential margin of clearance. Intersphincteric resections should only be recommended when in the preoperative staging procedure a minimum distance of the lower edge of the tumor to the dentate line is at least 0.5 cm and the carcinomas are classified uT1 or uT2 on ultrasonography. An infiltration of the puborectal sling is an exclusion criteria and only good or moderate differentiated tumor should be operated on by this procedure. If these parameters are not strictly considered, an increase of locoregional recurrences is unavoidable. Therefore, it is very important that experienced colorectal surgeons make the decision for selecting the right procedure.

In the beginning until 2002 in a relevant number of patients the tumor front did not reach the circumferential margin (R0 according to the definition of the UICC). However, the distance was certainly sometimes less than 1 mm which is known to lead to a high rate of local recurrences. Only after routine neoadjuvant radiochemotherapy in these patients, it decreased. Nevertheless it was still too high because the majority of these tumors were staged to be T2 cancer. In this context the peranal transsection of the rectum in the beginning of the procedure with exposure of the tumor close to the intersphincteric tissue for maybe two hours may have also contributed to the high rate of recurrence. A "sterilisation" by radiochemotherapy of the tumor may have a certain effect to reduce local recurrence.

Therefore interdisciplinary neoadjuvant treatment regimens must be forced in low and advanced tumors. Without doubt, this development has an important influence for selection of this specialized operative procedure and results in an increase of histopathological findings of ypT0 and ypT1 tumors in intersphincteric resections. In our experience, all patients with a proven carcinoma near the dentate line which could be potentially operated by intersphincteric resection should be treated by neoadjuvant preoperative radiochemotherapy.

Respecting all these parameters and characteristics in tumor and patient selection intersphincteric resection is a safe procedure regarding complication rates and prognostic outcome in the treatment of low rectal cancer and offers the very last option for sphincter preservation.

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Transanal abdominal transanal proctosigmoidectomy with descending coloanal anastomosis (the TATA procedure) for low rectal cancer treated with chemoradiation

John H. Marks, George J. Nassif, and Gerald Marks

Historically speaking, treatment of rectal cancer has been based on the stage of the tumor at presentation and its height in the rectum. In the past treatment was an abdominal perineal resection with end permanent colostomy. That being the case, it made perfect sense to measure tumors from the anal verge. This was typically done with a rigid sigmoidoscope so that a constant measurement could be obtained. Anatomically however, there is a high variability in the length of the anal canal. The canal itself can be anywhere from 5 mm to 5 cm in length depending upon the size and physique of the patient. The anal verge is where the epithelialized skin is encountered. The proximal margin of the anal canal is at the anorectal ring. The dentate line marks the midpoint. Therefore, a tumor at the 5 cm level measured from the anal canal could range anywhere in this location from the mid rectum to the upper aspects of the anal canal, depending on the anal canal length. It is for this reason that we and others have adopted the anorectal ring as the zero level so that physicians can compare apples to apples regarding the level of the tumor in the rectum itself. With the advent of high quality MRI, we are now able to measure with a reliable tool this anatomic location and level of the tumor from there [1]. That being said, a TATA procedure is an operation for cancers in the distal 3 cm, or lower 1/3, of the rectum.

The treatment of rectal cancer and the ability to take care of the cancer and avoid a permanent colostomy changed greatly with both the advent of preoperative chemoradiation and the ability of the TATA procedure to expand sphincter preservation. Clearly in a patient with rectal cancer, the first order of priority is to control the cancer with the highest quality of life. By avoiding a permanent colostomy, these patients certainly note a marked improvement in their quality of life and body image. To obtain the maximal benefit on downstaging of the cancer from the neoadjuvant chemoradiation, we base our clinical judgments on the cancer at the eight to twelve week mark following completion of chemoradiation. This allows for maximum benefit of downstaging. In considering what is being proposed and spoken of here, it is well to evaluate some of the largest international rectal cancer trials of the last decade to gain a sense of permanent colostomy rates. As a benchmark in the last large rectal cancer trial completed in the USA, NSABP R-03 Trial [2], abdominoperineal resections were carried out in 67% of the patients treated with no neoadjuvant therapy and in 50% of patients treated only with preoperative radiation therapy. While this study suffered from a low accrual rate, including only 116 patients, it does serve as a benchmark for where we have been in the United States not so long ago. The Swedish Rectal Cancer Trial, which involved 1168 patients, using preoperative radiotherapy, the APR rate was 55% [3]. The Norwegian Rectal Cancer Group published oncologic outcomes after TME resection and involving 2136 patients, and the abdominoperineal rate was 38% [4]. Similarly in the Dutch Colorectal Cancer Group involving 1805 patients, and the APR rate was 32% [5]. The aggregate of these studies included 4,849 patients and the overall abdominoperineal rate was 39% with only 33% of the patients having cancers in the distal 5 cm of the rectum. It is imperative that one remains mindful of these figures as the reader considers what is presented both in our chapter as well as throughout this book.

With the advent of preoperative chemoradiation for rectal cancer, the significant downstaging that is encountered has expanded surgical options for the rectal cancer surgeon. Significant regression in the cancer as well as complete response rates have been reported ranging anywhere from 12 to 28% [6]. As for the extension of sphincter preservation, the technical demands on the surgeon are quite different. The technical challenges

Table 1: Possible keys to extending sphincter preservation in rectal cancer management program

High dose radiation therapy (≥5500 cGy)
Accepting distal margins of 5 mm
Extended waiting period for surgery (8–12 weeks)
Decisions based on cancer after radiation therapy
Only fixed cancers in distal 3 cm – APR
TATA

Table 2: TATA = Transanal Abdominal Transanal

Advantage:
Known distal margin
Facilitates precise distal dissection
Removes challenge of impalpable scar after chemoirradiation for clamp placement
Know preoperatively if we will be able to spare the sphincter

presented by an anastomosis are dramatically different than those presented by a low anterior resection. At the heart of the matter from an oncologic standpoint, is what represents an adequate margin for distal rectal cancer. Historically, a 5 cm rule for a distal margin was advocated and then in the last decade, a 2 cm rule was adopted. More recently questions have been whether a margin of 1 cm or less is adequate, so long as it is R0 in nature. The challenge with all of this data is that the information is generally based on cancers that have not been treated with neoadjuvant therapy (Table 1).

In a longstanding rectal cancer management program that dates back to 1976 at Thomas Jefferson University Hospital, several keys were developed to extend sphincter preservation as part of a comprehensive multimodal rectal cancer management program. This program was the first of its kind to utilize preoperative radiation therapy and sphincter preserving surgery, using a long course of external beam radiation therapy, with a preferred dose of 5580 cGy [7–11]. Additionally, for low rectal cancers that would otherwise require a permanent colostomy, we have accepted a policy of distal margins that are as small as 5 mm in length. For the last decade, we have extended the waiting period after neoadjuvant therapy, first from 4–6 weeks to 6–8 weeks and now preferably from 8 to 12 weeks pushing all the way out to 12 weeks for the most distal cancers. Most importantly, the decisions based on sphincter preservation versus permanent colostomy are on the status of the cancer after completion of neoadjuvant radiation therapy [12]. With this in mind, we only recommend permanent colostomy for fixed cancers residing in the distal 3 cm of the rectum relative to the anorectal ring. For cancers that are mobile after radiation in the distal 3 cm, we advocate the TATA technique to technically accomplish sphincter preservation [13, 14].

The TATA procedure is Transanal Transabdominal radical proctosigmoidectomy with coloanal anastomosis. This was first developed in 1984 in the cadaver lab at Thomas Jefferson University by Dr. Gerald Marks. The operation itself starts transanally and then is followed by an abdominal phase, then a transanal phase to complete the anastomosis. The advantages of this approach are multiple (Table 2). First this allows a known distal margin relative to the cancer. This facilitates a precise distal dissection, which is especially important after the downstaging of chemoradiation. It removes the challenge to the surgeon with impalpable scar after chemoradiation for application of a clamp or a TA stapler from above. Lastly and what is perhaps most important in treating these patients is that it allows the surgeon to know preoperatively definitively whether they will be able to spare the sphincter.

With this approach in a three decade experience of over 750 patients, we have been able to accomplish sphincter preservation in 93% of our patient population.

Technical description

The operation is started with the patient in the extended lithotomy position. The anal canal is everted with Alice Adair clamps. We avoid the Lone Star retractor because of problems with injury to the surgeon's fingers during the intersphincteric dissection by way of the hooks. In an effort to limit blood loss, the operation is started by injecting through the gluteals and ischiorectal fossa into the levators with Lidocaine-Epinephrine solution. The incision is made through the mucosa at the level of the dentate line circumferentially with the electric cautery. This is a very important step as it avoids splitting of the rectal wall as the dissection is carried out. Once this is completed, Metzenbaum scissors are used to spread in the posterior midline through the full thickness of the internal sphincter, which represents the continuation of the inner circular layer of the muscularis propria of the rectum. By spreading posteriorly the glistening white of the puborectalis is seen and this is what shows the surgeon they are in the proper inter-sphincteric plane. The Metzenbaum scissors are used to incise the muscular wall of the internal sphincter in a full thickness fashion keeping perpendicular to the axis of the rectum (Fig. 2). In this fashion, the inter- sphincteric plane between the transected distal rectum and the puborectalis is entered into. Small Deaver retractors are placed in to this plane and once started in the proper plane, it is easy to carry out the dissection going cephalad [15] (Fig. 3). The surgeon must

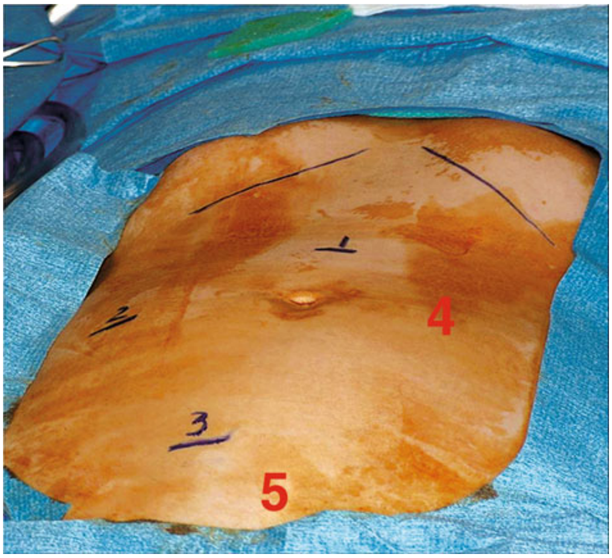

Fig. 1. Port placement for laparoscopic TME/TATA

be careful not to go too deep, in which case the levators will be violated with consequences in terms of function (Fig. 4). If the dissection veers superficially, the rectal wall will be violated and the oncologic procedure irreparably damaged. Dissection is taken cephalad to the level of the seminal vesicles in the male or the level of the cervix in the female. Care must be taken anteriorly in the male to assure that the dissection is not inadvertently taken anterior to the prostate. Typically, it is the anterior portion of the operation that is the most challenging. Unless there is a bulky tumor, and then this is approached last. Approaching anterior last allows the dissection to be brought from two directions and better orients the surgeon regarding depth of dissection. Once the rectum has been mobilized circumferentially as high as could be comfortably performed, a Vicryl stitch is used to turn in the rectum in a watertight fashion. The pelvis is irrigated and E-tape and Tegaderm is applied. While the first phase is transanal, the second phase is a laparoscopic abdominal portion.

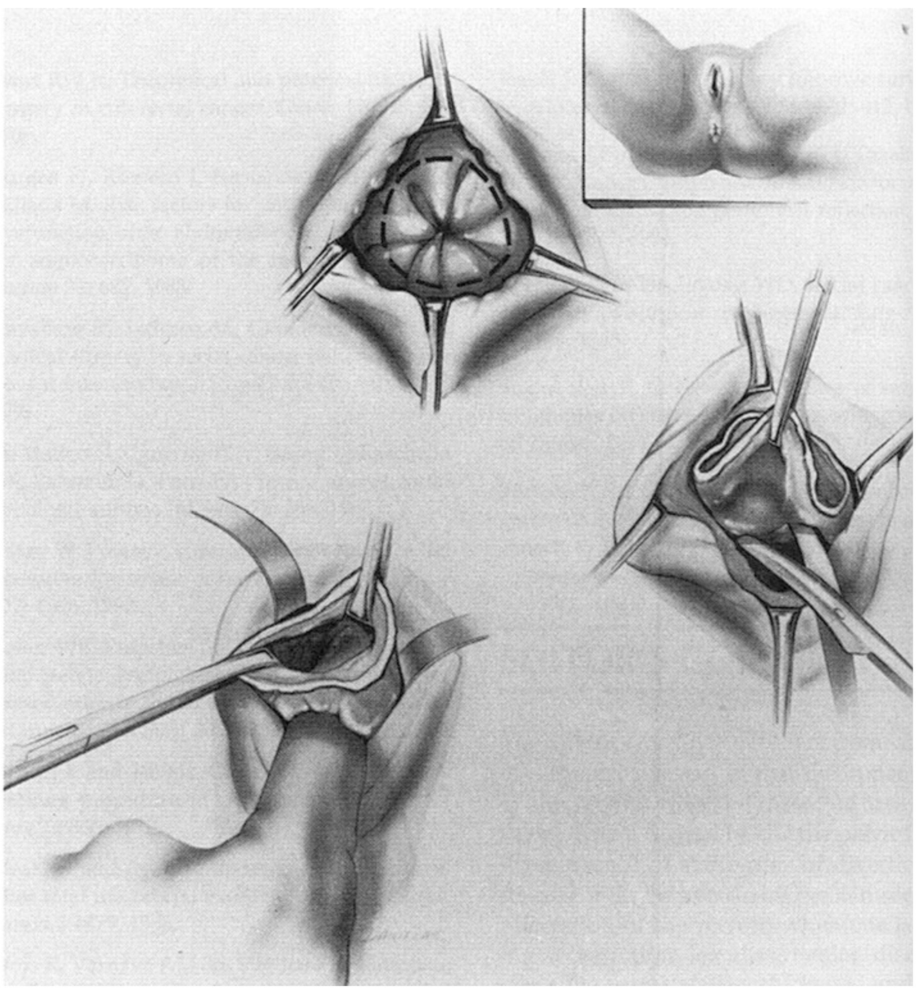

Fig. 2. Transanal portion of TATA (inset: patient positioning) Top – incision at dentate line, right – sharp dissection, left/bottom – blunt dissection

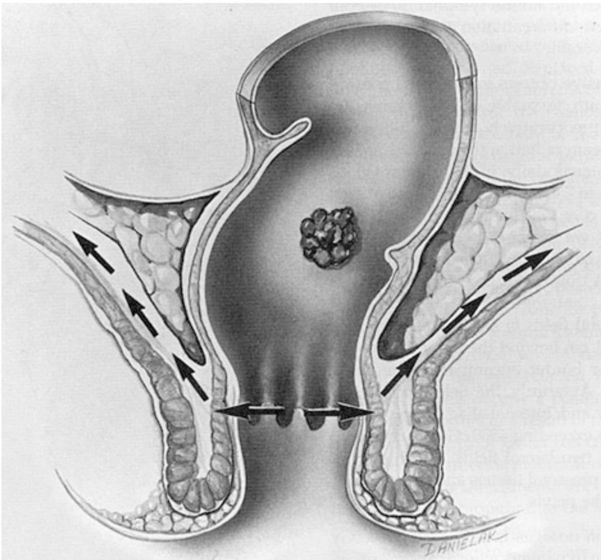

Fig. 3. Intersphinteric plane

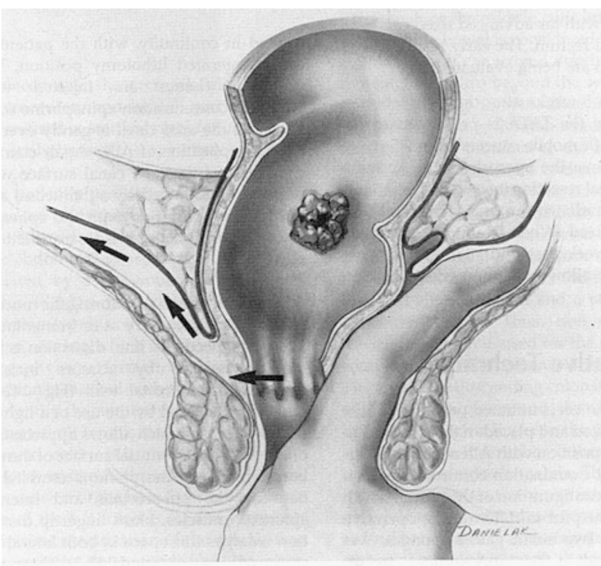

Fig. 4. Intersphinteric plane with blunt dissection

Abdominal portion of operation

The abdominal operation consists first of a thorough exploration. The procedure has both an abdominal part of the operation and the pelvic part of the dissection. These aspects of the operation are generally performed now laparoscopically. The trade off with laparoscopy is improved visualization at the cost of a diminution of tactile sensation. This highlights the benefit of high definition camera and good light source and the keeping of a bloodless field. The immediate control of any bleeding is of paramount importance in complex abdominal laparoscopic surgery, as even small amounts of blood absorb a great deal of light and decrease the visibility of the field. The liver is inspected fully and the abdominal portion of the operation is begun.

Abdominal portion

The port positions used for the laparoscopic procedure are shown in Fig. 1 and are carried out in the technique as described in Huscher [16]. The important aspects of the abdominal operation are as follows:

1. Wide mobilization of the splenic flexure.
2. Positioning of the small bowel away from the pelvis
3. High ligation of the IMA and IMV
4. Mobilization along the line of Toldt.

Once exploration is carried out, the laparoscope is placed in the Number 1 port for direct visualization down the transverse colon. The patient is put in a reverse trendelenburg position, right side down. The gastrocolic ligament is incised with a LigaSure. Entry into the lessor sac is carried out and the greater omentum is transected out to the splenic flexure. The upper portion of the Line of Toldt is mobilized. The mesentery of the transverse colon is released approximately one centimeter inferior to the lower border of the pancreas. In this way transverse and descending mesentery are separated from their attachment to the retroperitoneum and Gerota's fascia. The patient is then put in steep trendelenburg, right side down to help position the small bowel out of the field. The dissection is carried out in a medial to lateral fashion. The retroperitoneum is incised from the sacral prominence up to the duodenal jejunal junction. The hypogastric nerves are the key to the dissection. They are identified and displaced posteriorly. This both protects the nerves and puts one in the proper plane where the left ureter is immediately identified. The IMV is dissected out above the IMA, and the retroperitoneum is displaced posteriorly. The IMA is freed circumferentially. Once this is done and the left ureter has been identified, the IMA can safely be transected. The IMV is then transected immediately inferior to the pancreas and in this fashion, vascular control is obtained. The abdominal portion of the operation concludes with full mobilization of the sigmoid and descending colon long the Line of Toldt. At this point, attention is turned down to the pelvis.

Pelvic portion

The pelvic portion and the fundamentals of the pelvic portion of the operation are comprised by the concept of three-dimensional retraction as well as the four steps of opening the box and performing a posterior lateral then anterior dissection to complete the resection itself.

The port sites have already been demonstrated and the concept of three-dimensional retraction are as follows: Left hand in port 1 is used to pull the rectum cephalad. The camera comes in through port 2. Port 3 is actually the working hand of the surgeon. Port 4 in the left lower quadrant is used to retract anteriorly along the rectovesical fold much in the same way as a St. Marks retractor would be done in open surgery. Port 5, which is immediately suprapubically, is employed opposite or wherever the dissection is being carried out in order to create a retraction of the pelvic sidewall opposite the mesorectal envelope. Typically a suction irrigator is used through here to create counter traction to the area being excised to perform a total mesorectal excision. The dissection in the pelvis is best carried out utilizing scissors. The scissors tips and the electrocautery are more precise than other devices. The electrocautery is used to then "open the box" by incising down the right and left perirectal sulcus and joining anterior in the Pouch of Douglas or the rectovesical fold. Once this is done, the second step is a posterior dissection. Care is taken to be certain that one is anterior to the hypogastric nerves. The posterior dissection is facilitated by having the suction irrigator coming in through Port 5 as a retractor anterior to the mesorectum. A sharp mesorectal incision is carried out by following immediately anterior to the hypogastric nerves on the right and left side then the section is taken down posteriorly to the puborectalis, which connects to the dissection from below. It is not uncommon to find a small gush of fluid as one enters into this space. Having completed this, the next step is the lateral dissection along the right and then the left sides of the mesorectum. The hypogastric nerves are followed in order to make sure the surgeon stays in the proper plane of dissection as the standard in TME surgery. The sucker, which is serving as a lateral retractor to carry out three-dimensional retraction, is used on the pelvic sidewall and then the dissection is brought around anteriorly. Typically at this point, one connects into the dissection from below. This greatly facilitates the remainder of the dissection. The middle rectals when present can be taken with the LigaSure and this completes the total mesorectal excision. The TME specimen is retracted out of the pelvis into the abdomen. At this point, the pelvis is completely dissected and with all areas visible perfect hemostasis can be addressed. The view of the upper aspect of the transected anal canal can be obtained and then frequently, unless there is a very bulky tumor, the tumor can be delivered transanally. Once this is done, either a colonic J-pouch or direct hand sewn coloanal anastomosis is carried out. Having completed this portion, the specimen is inspected, gowns and instruments are changed. We go back abdominally. The abdomen is explored to make sure it is hemostatic and that the colon has been brought down in proper orientation, not twisted. Then a diverting loop stoma with an ileostomy or transverse loop colostomy are created.

Overall results

While reading these results, it is well to be mindful that the data presented comes from an experience of approximately 1700 minimally invasive colorectal cases and 1100 rectal cancer patients. This is mentioned only to accentuate the need for expertise in the treatment of rectal cancer as well as minimally invasive surgeons to apply these approaches.

Our overall experience with the TATA procedure for rectal cancer includes 326 patients, with 145 performed laparoscopically. We first compared the outcomes of 200 rectal cancer patients resected laparoscopically, and case matched to open rectal cancer resection. In this group, the laparoscopic completion rate was 87% before 2001 and 92% after 2001. When we looked at sphincter preservation rate, there was no difference between the laparoscopic or the open cohort. Both of these sphincter preservation rates were 93%. With a mean follow up of 34 months in this group of patients, the overall local recurrence rate was 1.9%. The recurrence rate in the laparoscopic group was 1.8% with a follow up of 23.9 months (range is 1.8 to 89.5 months). In the open group, local recurrence rate was 2.1% with a mean follow up of 49.2 months (2.3 to 99.9 months) ($p > 0.05$). Satisfied that there was no difference in the major oncologic outcomes in a comparison of the laparoscopic to the open group. We looked at a group of patients who underwent laparoscopic TATA resection following neoadjuvant therapy for rectal cancer at the distal 3 cm [17]. This looked at our experience over a ten year period from 1998 to 2008 performing laparoscopic TATAs. 54 of the patients were men, 25 were woman. Mean BMI was 26.5 with a range of 5.2. The tumor level (relative to the anorectal ring) was 1.2 cm ranged from -5 mm to 3 cm in size. Median radiation dose was 5400 cGy. In looking at this group, the conversion rate was only 2.5%. The distal margin R0 resection rate was 98.7%. Overall, 90% of these patients live their life without a stoma. There were no mortalities and 11% major morbidity rate. This included two failed anastomosis requiring colostomy for full thickness rectal prolapse. We had one ischemic neo-rectum that was resected and two small bowel obstructions that were treated. Overall in this group, our complete response rate was 28% with 15% of the patients having ypT1 cancers, 28% of the patients having ypT2 cancers and 29% of the patients having ypT3 cancers. Overall, 82% of the patients were ypN0. With a mean follow up of 34.2 months, the local recurrence rate was 2.5% with a 97% Kaplan Meier five year actual survival.

Our favorable experience with this lead us to explore "an incisionless" laparoscopic proctectomy using the anal canal for delivery of the specimen. In looking at 106 TATA patients, compared 51 incisionless TATAs to 55 previous consecutive laparoscopic TATAs where the specimen was removed through a transverse incision in the right lower quadrant. In this group of transanal extraction sites, we noted no splenic flexure injuries, ureteral injuries and no conversions. The largest incision length of the incisionless TATA patients was 1.9 cm (1.2 to 3.0 cm) compared to 6.5 cm for a standard laparoscopic TATA (4.1 to 21 cm). Mean total length of all incisions in the incisionless group was 4.6 cm (1.8 to 8 cm) compared to 9.4 cm with the laparoscopic TATA 5.4 to 24.1 cm. Again, the local recurrence rate in the incisionless group was within the norm of our experience. The local recurrence rate was 2.0% with a distant metastatic rate of 3.9%.

Conclusion

In conclusion, we have presented to you our experience with TATA resections. In viewing this data, it is worth recalling that 100% of these patients had their cancers in the distal 3 cm of the true rectum. These cancers in the lower third of the rectum would almost always be approached with a standard, abdominal perineal resection. This is in keeping with the data presented earlier with the worldwide APR rate of 30 to 40%. That being said, 53% of these patients were tethered or fixed on presentation and 68% of the patients were men. All these factors present a highly unfavorable patient population both for cure and sphincter preservation. We were able to accomplish all of this with a local recurrence rate of only 2.5% and an overall survival of 91%. This approach offers hope for rectal cancer patients for sphincter preservation, even with cancers in the distal third of the rectum.

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Robot-assisted intersphincteric resection

Seon Hahn Kim and Jae Won Shin

The major benefits of laparoscopic colorectal surgery include; better cosmesis, less post-operative pain, earlier return of normal bowel function and shorter hospital stay without sacrificing oncological clearance. Despite its popularity, however, conventional laparoscopic surgery has its short comings such as a limited two dimensional views, limited dexterity of instruments within the confines of the abdominal space, fixed instrument tips and possible misalignment of hands and instruments. The preservation of anal sphincter function while obtaining an oncological clearance in very low rectal cancers can be very challenging. When performing a laparoscopic total mesorectal excision (Lap TME), meticulous and precise dissection of the mesorectum in a previously irradiated rectum down to the pelvic floor within the confines of a narrow pelvis, is a technical challenge even for experienced laparoscopic colorectal surgeons.

Intersphincteric resection is an acceptable alternative to abdominoperineal resection for very low rectal cancer close to the anal canal. A complete rectal dissection deep down to the upper anal canal from the above is a crucial part of the procedure in order to facilitate an easy and safe intersphincteric dissection from the bottom, particularly in males.

The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) was developed to overcome the short comings of conventional laparoscopic surgery. Compared with conventional laparoscopic surgery, the da Vinci system has several advantages such as three dimensional imaging, a stable camera and operating platform, articulating instruments with various degrees of freedom, excellent ergonomics and tremor free movements. All these aspects of the da Vinci system seem particularly beneficial to perform very low pelvic dissection. So many surgeons are optimistic that the robotic surgical system will overcome the pitfalls of laparoscopy, with resultant enhanced oncologic and functional outcomes.

Operation room setup, patient positioning, and port placement

After the induction of general anesthesia, the patient is placed in a modified lithotomy position with the legs apart on a bean-bag mattress to prevent any sliding. Six ports are used, including one 12-mm camera port, four 8-mm robotic working ports, and one 5-mm port for the assistant. A 12-mm trocar is placed through an incision on the right side of the umbilicus for the robotic camera. The intra-abdominal pressure is maintained at 10–12 mmHg. The first daVinci® 8-mm port (right lower quadrant (RLQ) port) is placed at the McBurney point. The second (right upper quadrant (RUQ) port) is inserted in the right subcostal area on the midclavicular line (MCL). The third (LUQ port) is

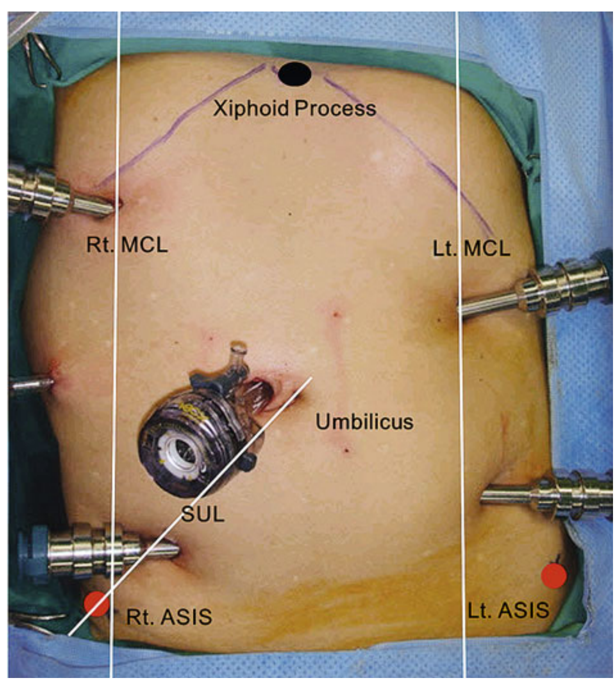

Fig. 1. The layout of the port placement for single-stage robotic intersphincteric resection. MCL _ midclavicular line; SUL _ spinoumbilical line; ASIS _ anterior superior iliac spine; Rt. _ right; Lt. _ left

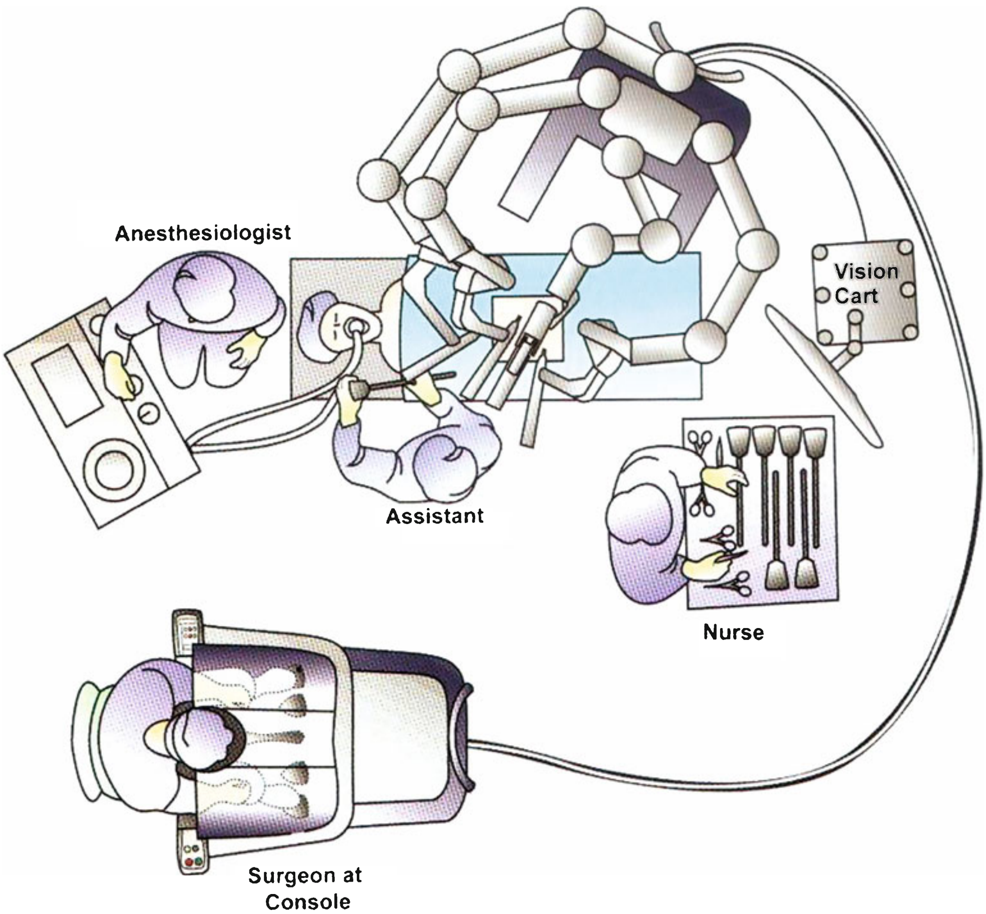

Fig. 2. An overhead view of the operation room configuration for robotic intersphincteric resection

placed in the left upper quadrant approximately 1 to 2 cm above the camera port at the crossing of the MCL. The fourth (LLQ port) is inserted in the left lower quadrant approximately 1 to 2 cm lateral to the MCL. These four ports are used for the robotic arms and are separated from each other by at least 8 cm. To allow the assistant access, a 5-mm trocar is placed in the right flank area, near the anterior axillary line, at the umbilicus level. This is used for suction/irrigation, clipping of vessels, and retraction of tissues. During the pelvic dissection stage, the assistant uses the RUQ port as well, therefore maximizing assistance by use of both hands. The port placement is seen in Fig. 1. An overhead diagram of the operation room configuration for robotic intersphincteric resection is also seen in Fig. 2.

The surgical procedure

The surgical procedure is comprised of 4 stages:

Phase 1. Vascular ligation, and sigmoid colon to splenic flexure mobilization

The patient is tilted to the right side and placed in the Trendelenburg position. The small-bowel loops retracted out from the pelvic cavity to the RUQ to expose the inferior mesenteric artery (IMA). Before applying the robot system, the whole abdominal cavity is explored by use of laparoscopic instruments. The robot cart is positioned obliquely at the left lower quadrant of the abdomen along the imaginary line from the camera port to the

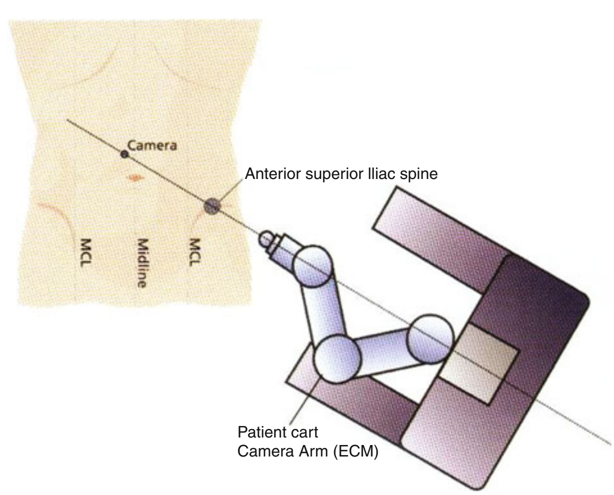

Fig. 3. Correct roll up angle for patient cart docking

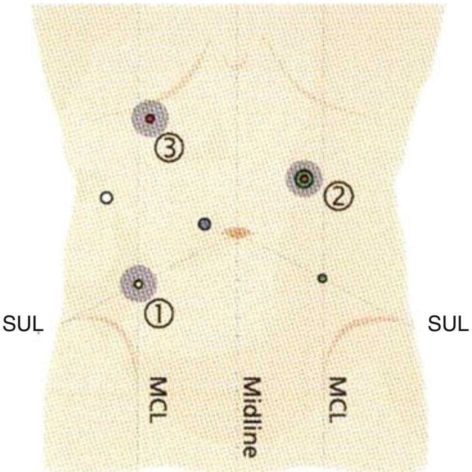

Fig. 4. Robotic arms ①, ② and ③ aligned for the 1st phase

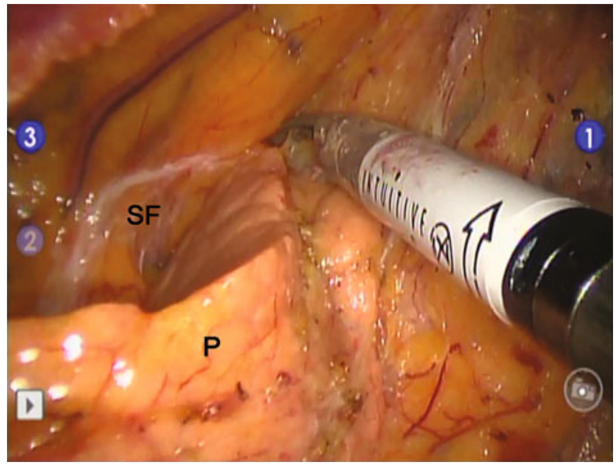

Fig. 6. The pancreas (P) is separated by entering the lesser sac (LS) from the medial approach. This is an essential step for complete takedown of the splenic flexure

anterior superior iliac spine (Fig. 3). Then, the robotic arms are docked to the trocars. A zero-degree robotic camera is used. A monopolar curved scissors is used by the RLQ arm as the surgeon's right hand. A Maryland bipolar grasper forceps is taken by the RUQ arm as the surgeon's left hand, and a Cardiere grasper is used by the LUQ arm as the surgeon's second left hand. In this phase, the LLQ port is not used (Fig. 4). Initially, the mesocolon over the IMA is retracted upwardly with a Cardiere forceps. The peritoneum around the base of the IMA is incised and dissected with a monopolar scissors. The periaortic hypogastric nerve plexus is carefully preserved (Fig. 5). The IMA is divided near the root (high tie) with Hem-o-lok® clips (Weck Closure System, Research Triangle Park, NC) or Robotic Hem-o-lok® clips. The inferior mesenteric vein is identified by dissecting superiorly toward the ligament of Treitz, and is divided near the inferior border of the pancreas. The medial dissection continues laterally until the left colon is separated from the retroperitoneum, and superiorly over the pancreas until the lesser sac is entered (Fig. 6). The left gonadal vessels and the ureter are identified and preserved. Lateral detachment is initiated along the white line while the sigmoid colon is retracted medially by the assistant. The lateral counter-traction by the LUQ arm assists a safe dissection. The lateral dissection continues cephalad to the proximal part of the descending colon. In this phase, the robot can be set up with a three-arm system (including camera) by temporarily dedocking the LUQ arm when external collision with the RLQ arm occurs, in particular, in small patients. The lateral detachment continues up to the splenic flexure. The omentum is detached from the transverse colon. The transverse colon is pulled down caudally by the assistant, and the omentum is pulled up by use of the RUQ robotic arm. The renocolic and splenocolic ligaments are divided, and the splenic flexure is fully mobilized (Fig. 7).

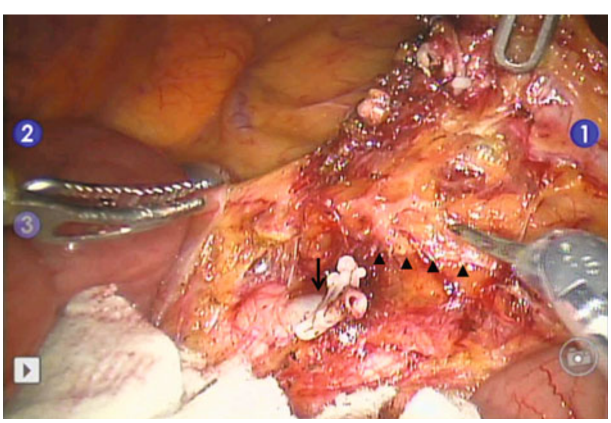

Fig. 5. Division of the inferior mesenteric artery at the root (arrow), with preserving the aortic nerve plexus (arrow heads)

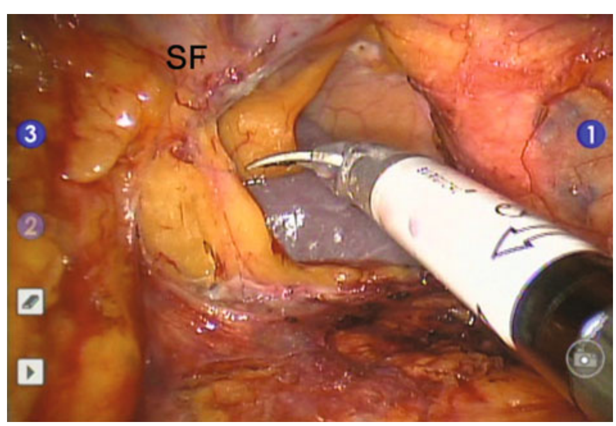

Fig. 7. The splenic flexure colon (SF) is accessed laterally and freed from the spleen

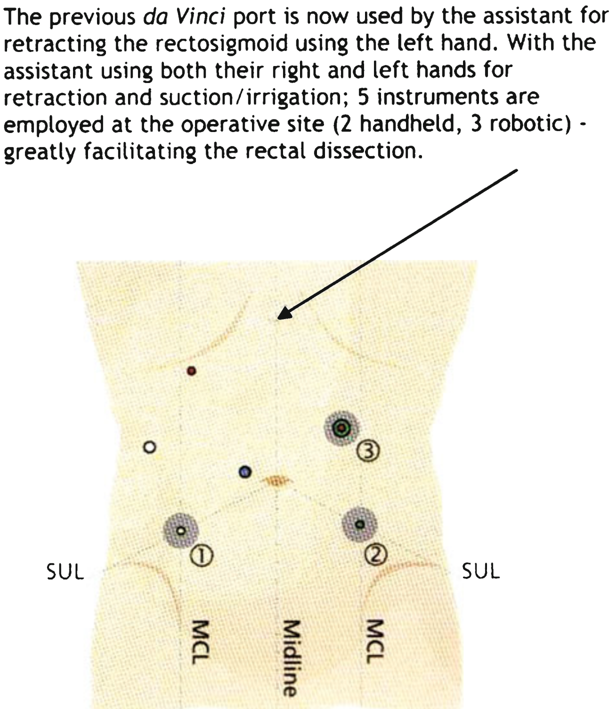

Fig. 8. Robotic arms ①, ② and ③ aligned for the 2nd phase

Phase 2. Pelvic dissection
The robotic instruments of the RUQ and LUQ ports are dedocked and redocked to the LUQ and LLQ ports, respectively (LUQ _ Maryland forceps; LLQ _ Cardiere forceps) (Fig. 8). Now, the assistant uses the RUQ port to cephaladly retract the rectosigmoid colon and the 5-mm port for suction and/or retraction. Therefore, five instruments are used in the operative field (three robotic and two handheld), maximizing assistance for TME. With the rectosigmoid colon retracted cephalad, the robotic Cardiere grasper retracts the rectum anteriorly, thus exposing the plane between the mesorectal fascia and the inferior hypogastric nerves. An avascular space between the mesorectal fascia and the presacral fascia is sharply dissected with a monopolar scissors (Fig. 9). The inferior hypogastric nerves and, distally, the pelvic nerve plexus are identified and preserved. Because the small bowel would obscure the right lateral plane, further posterior dissection down to the levato ani muscle is approached from the left lateral plane, while the rectum is lifted up by the Cardiere graspers. The left lateral dissection is performed while the rectum is drawn to the right side by the assistant. Then, the right lateral dissection is completed in a reverse fashion of rectal retraction. Finally, the anterior dissection is performed by incising the peritoneal reflection. Sharp dissection continues to develop the correct plane between the rectum and vagina/seminal vesicles prostate. The rectum is retracted downward with the second robotic instrument (Maryland

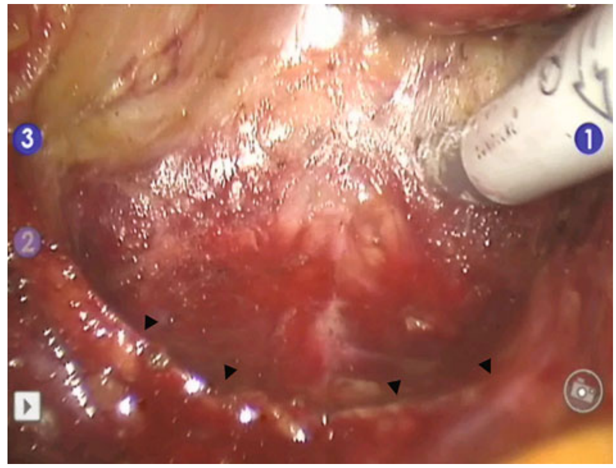

Fig. 9. Posterior dissection between the mesorectal fascia and the presacral fascia. The Waldeyer's fascia (arrow heads) is opened by a sharp dissection

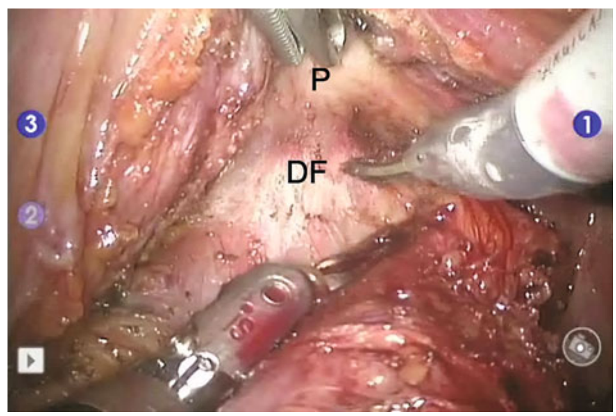

Fig. 10. Anterior dissection between the rectum and the prostate (P).The Denonvillier's fascia (DF) is clearly visualized

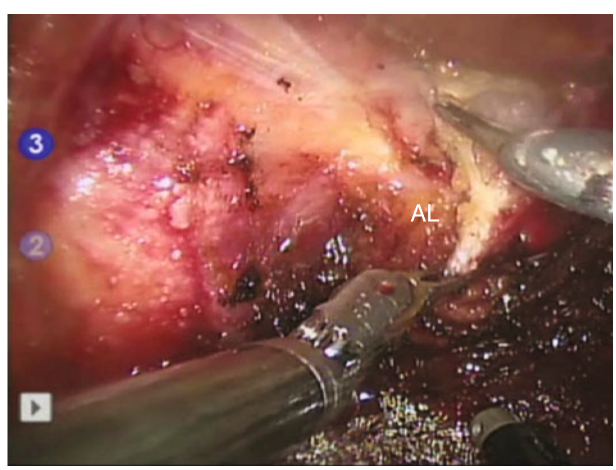

Fig. 11. Deep posterior dissection between the rectum and the pelvic floor. The anococcygeal ligament (AL) is clearly visualized

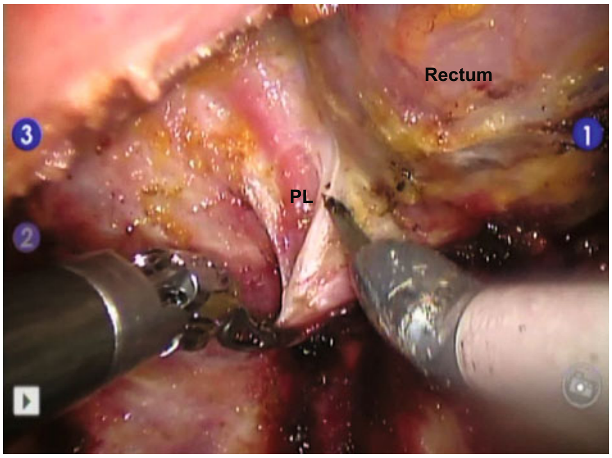

Fig. 12. Deep lateroposterior dissection between the rectum and the puborectalis muscle. The left sling of the puborectalis muscle (PL) is clearly visualized

grasper), and the vagina/prostate are counter-retracted upward with the third instrument (Cardiere forceps) (Fig. 10). The pelvic dissection was performed to the level of the pelvic floor and included division of the anococcygeal ligament posteriorly, puborectalis muscle laterally and dissection of Denonvillier's fascia anteriorly, which was crucial for the intersphincteric dissection in the following step (Figs. 11 and 12).

Phase 3. Transanal intersphincteric dissection

Once the pelvic dissection was complete, the robotic instruments were disengaged, and the cart was moved away. The patient's hips were hyperflexed to allow better access to the perineum. During transanal dissection, the rectum was packed with a moist gauze to avoid intra-operative seeding of malignant cells. A circumferential incision of the mucosa and the internal anal sphincter was performed just above the dentate line in order to obtain at least 10 mm distal margin. With careful circumferential dissection between the internal anal sphincter and the external anal sphincter/the levator ani muscle, the level of the robotic pelvic dissection was reached.

Phase 4. Rectal reconstruction and loop ileostomy

The rectum and the sigmoid colon are delivered and transected via the anal canal. Sometimes if the tumor is too big or the mesentery is too thick to deliver through the anus, the specimen is delivered via a minilaparotomy incision on the left lower quadrant port. After transection of the specimen, reconstruction of bowel continuity was performed using an end-to-end or side-to-end procedure, a colonic J pouch, or a coloplasty via a handsewn coloanal anastomosis with absorbable interrupted sutures. Finally, a loop ileostomy was created in the area of the right lower quadrant port, and suction drainage was inserted in the pelvic cavity.

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Postoperative function

Quality of life following rectal resection

Brigitte Kovanyi-Holzer

Introduction

Since the introduction of abdominal perineal excision (APR) by Ernest Miles in 1908 and the concurrent demand for radical resection of the tumor-bearing rectum, nearly 43 years elapsed before Goligher first expressed concern regarding the sequelae of surgical problems in the course of tumor resection affecting patient's quality of life (QOL) [1, 2].

Today it is widely accepted that most patients with rectal cancers or disorders that will require surgical therapy can be treated with sphincter preservation by standardized surgical techniques [3]. Although the lowest rates of abdominoperineal resection (APR) and consequent permanent stoma formation have been reported to be between 9 and 10% in specialized units, observation of multicenter studies have shown significantly higher numbers of patients who undergo APR (37–68%) [4]. In the past, many publications have dealt with the sequelae of APR and the presence of a permanent colostomy, and it is widely accepted that this procedure involves a heavy price for affected patients [5–9]. However, with the advent of circular surgical stapling devices as well as following the introduction of intersphincteric resection low colorectal and coloanal anastomoses have become routine without any compromise in oncological outcomes.

In an earlier study we compared the quality of life (QOL) of patients after intersphincteric resection with that after anterior resection. There were no significant differences in the domains food, work, social function, sexual life, mobility, spare time activities, subjective quality of health, and subjective quality of life [3].

Social well-being

Social life may deteriorate after surgery for rectal cancer, although results are contradictory. A colostomy may bring a fear of being a nuisance to other people, mainly because of odour, and there may be embarrassment about the presence of a stoma.

Wirsching et al. in 1975 examined a group of 214 patients who had a permanent colostomy and a group of 110 who had restorative surgery [10]. There was significantly reduced social contact in the colostomy group. Similarly, MacDonald and Anderson in 1985 noted that those with a colostomy tended to participate less in social activities than those without a stoma; their interests in outdoor pursuits were significantly less [11].

In 1984 MacDonald and Anderson found a worsening partner-relationship in 29 per cent of patients with a colostomy compared with 14 per cent of those who had a sphincter-saving resection [12].

Psychological well-being

There are some studies showing a high prevalence of psychological problems in patients operated for rectal carcinoma, even though the instruments used in most cases may not be psychometrically reliable. Patients with colostomies tend to suffer most.

Devlin et al. in 1971 found that 23 per cent of 83 patients suffered from a severe form of psychological disturbance after APR, compared with one of 37 patients who had a sphincter-saving operation [13].

In 1983 Williams and Johnston reported a 32 per cent prevalence of depression following an APR, compared with a 10 per cent prevalence after anterior resection [14].

In 1975 Wirsching et al. used the Heidelberg Colostomy Questionnaire in a study which covered mainly social and psychological function in patients with a stoma. They evaluated that the colostomy was associated with a significant degree of depression, hopelessness, loneliness and suicidal thoughts [10].

Similarily, patients after APR studied by MacDonald and Anderson were found to have a statistically significant higher incidence of low self esteem and feelings of stigma than those who had undergone a sphincter-saving resection [10].

Despite these findings, there has been some controversy among surgeons about the real impact of a permanent colostomy on patient quality of life (QOL). Since some data show that a permanent colostomy may even be more beneficial for patient QOL than a very low sphincter-preserving anterior resection [8].

On the explanations for these contradictory observations could be differences in the definition of QOL as well as the instruments used to evaluate it.

"Quality of life" may be regarded as representing one individual's ability to carry out daily acitivities, as well as satisfaction with personal performance and with the balance between disease control and adverse effects of treatment [15, 16]. However, our own experiences as well as the observations of others indicate that QOL following the therapy of a certain disorder is influenced by various other factors than by the treated disease alone.

Preoperative expectations

The patient's expectations in regard of the disease and the proposed operation appear to be of major importance for his/her subjective perception of the outcome of treatment.

What does the patient expect from the operation? Apart from the primary desire to achieve cure from the disease, other expectations on the part of the patient can only be surmised.

In a prospective study we evaluated the patient's preoperative expectations as objectively as possible and to describe the patient's priorities in relation to age, gender and socio-economic status.

In the period from 1998–2001, 167 patients were evaluated by a questionnaire consisting of 15 questions prior to surgery for colorectal cancer [17]. The questionnaire included various aspects that were thought to influence the patient's quality of life. Moreover, the patients were given the opportunity to rate the questions they considered most important.

The following five items were considered most important by the total group of patients: Complete cure of the disease (98%) followed by the avoidance of a stoma (93%), undisturbed continence (90%), less pain (54%), normal digestion (42%) and good control over bowel evacuation (41%).

In contrast, the following aspects were considered less important by the patients: the ability to eat as desired (43%), to use public transport (29%) or to attend public events (27%).

Cure from the disease – rated most important by the total group – was given significantly less priority by patients older than 80 years of age compared to those younger than 79 years of age ($p = 0.0065$).

To have an operation without a stoma was significantly less important for patients aged 28 to 50 years compared to those older than 51 years ($p = 0.0144$).

An evaluation of the data in relation to the education level revealed that patients who had attended school for more than 12 years gave less importance to the problem of a colostomy ($p = 0.061$). These patients considered it very important to avoid adjuvant treatment ($p = 0.0087$), and also gave more importance to the ability to resume work early ($p = 0.0061$).

The patients' expectations prior to the start of treatment for colorectal carcinoma appear to depend on several individual factors. In our prospective trial, age and the level of education influenced various questions to a differing extent (Table 1).

Furthermore, Solomon et al. described that patients' preferences do not always accord with those of clinicians [18]. Unless patients' preferences are explicitly sought and incorporated into clinical decision making, patients may not receive the treatment that is best for them. In a prospective study patients undergoing curative surgery for colorectal cancer were interviewed postoperatively to elicit their preferences compared with those expressed by clinicans.

Table 1

Priorities according to gender (mean)

Priority	Female	Male	Total
Cure of the disease	4.3*	4.4	4.3
No stoma	3.8	3.8	3.8
Normal digestion	1.98	1.58	1.76
Control of stool evacuation	1.58	1.48	1.52
No pain	2.06	1.99	2.0

*5 = most important, 1 = less important.

Priorities according to age (mean)

Priority	28–50 years	–60	–70	–80	>80	*p*
Cure of the disease	4.7	4.1	4.3	4.6	3.7	0.0065
No stoma	2.7	3.9	4.1	3.6	4.3	0.0144
An undisturbed sexual life	0.2	0.3	0	0	0	0.0033
Being able to eat as desired	0.0	0.1	0.6	0.7	0.4	0.011

Priorities according to education (number of school years) (mean)

Priority	<9 years	9–12	>12	Total	*p*
No stoma	4	4.1	3	3.87	0.0061
No adjuvant treatment	0.09	0.39	0.96	0.38	0.0087
Being able to resume work early	0	0.03	0.78	0.15	0.0061

Table 2

Total	**257 patients (%)**
Male	149 (58%)
Female	108 (42%)
Age (median, min, max)	63.5 (17–91) years
Educational status	
No high school	97 (37%)
High school	65 (25%)
College or university	71 (28%)
Missing data	24 (10%)
Geographic origin	
North Europe (Copenhagen, Aarhus, Goeteborg)	81 (32%)
Middle Europe (Erlangen, Luebeck, Krakow, Nantes, Geneva, Vienna)	113 (44%)
South Europe (Barcelona, Padua, Ankara)	25 (10%)
Arabian or Asian origin (Alexandria)	29 (12%)
Missing data	9 (2%)

Life style	**Median**	**Min-Max**	***p* value**
Sex			
Male	3.2	1–4	
Female	3.16	1–4	0.738
Age			
≤63 years	2.88	1–4	
>63 years	3.4	1–4	0.0001
Educational status			
No high school	3.1	1–4	
High school	3.25	1–4	
College or university	3.44	1–4	0.246
Geographic origin			
North Europe	3.70	1–4	
Middle Europe	3.10	1–4	
South Europe	3.0	1–4	
Arabian or Asian origin	1.6	1–3.5	

Coping/behaviour	**Median**	**Min-Max**	***p* value**
Sex			
Male	3.0	1–4	
Female	3.11	1–4	0.729
Age			
≤63 years	2.82	1–4	
>63 years	3.24	1–4	0.0001
Educational status			
No high school	3.0	1–4	
High school	3.11	1–4	
College or university	3.11	1–4	0.4440
Geographic origin			
North Europe	3.5	1–4	
Middle Europe	3.0	1–4	
South Europe	3.11	1–4	
Arabian or Asian origin	1.3	1–3.5	0.00001

Depression/selfperception	**Median**	**Min-Max**	***p* value**
Sex			
Male	3.17	1.17–4.0	
Female	3.0	1–4	0.379
Age			
≤63 years	3.0	1–4	
>63 years	3.2	1.17–4.20	0.003
Educational status			
No high school	3.0	1–4	
High school	3	1.5–4	
College or university	3.17	1–4	0.273
Geographic origin			
North Europe	3.67	1.8–4	
Middle Europe	3	1.1–4	
South Europe	3	1–4	
Arabian or Asian origin	2.14	1–4	0.00001

p value: n.s.

Embarrassment	**Median**	**Min-Max**	***p* value**
Sex			
Male	3	1–4	
Female	2.67	1–4	0.536
Age			
≤63 years	2.67	1–4	
>63 years	3.33	1–4	0.00001
Educational status			
No high school	2.67	1–4	
High school	3	1–4	
College or university	3	1–4	0.389
Geographic origin			
North Europe	3.33	1–4	
Middle Europe	3	1–4	
South Europe	2.67	1–4	
Arabian or Asian origin	1.33	1–4	0.00001

There were significant differences between patients and clinicians. Clinicians were more willing than patients to trade survival to avoid a permanent colostomy in favour of chemoradiotherapy. Patient's strongest preference was to avoid chemotherapy, more than to avoid a permanent colostomy [18].

QOL instruments

As mentioned above, controversial results of the impact of a permanent colostomy on the patient's QOL can be partly explained by differences in quality of life instruments that were used, as well as by differences in patient populations [8,19].

Generic questionnaires, such as the Nottingham Health Profile, are useful and allow the researcher to compare QOL across whole patient populations [20]. However, they may not be sensitive enough to measure changes in QOL which may be brought about by different types of surgery or adjuvant treatment.

Questionnaires which have been designed for use in patients with cancer, such as the Rotterdam Symptom Checklist and the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C 30 core questionnaire, may be more suitable. In addition, further questionnaires specific to colorectal cancer are necessary. For example, the EORTC group developed a colorectal cancer questionnaire or module (QLQ-CR 38), which has been validated in the Netherlands and is being tested in a number of international phase III trials.

In a recent multicentric trial focusing on QOL aspects in patients with a permanent colostomy we have modified a validated instrument for QOL measurement in patients suffering from fecal incontinence. For this purpose the QOL questionnaire for fecal incontinence introduced by Rockwood et al. of the American Society of Colorectal Surgeons (ASCRS) was adapted by simply replacing the term "incontinence" by "colostomy". A pilot study confirmed the applicability of this instrument was performed and the questionnaire proved to be easily understandable although there is still a lack of a validation process for the specific use in patients with a stoma [21].

Social factors (education, religion)

We felt that the patient's existing social and cultural situation might strongly effect the QOL outcome after

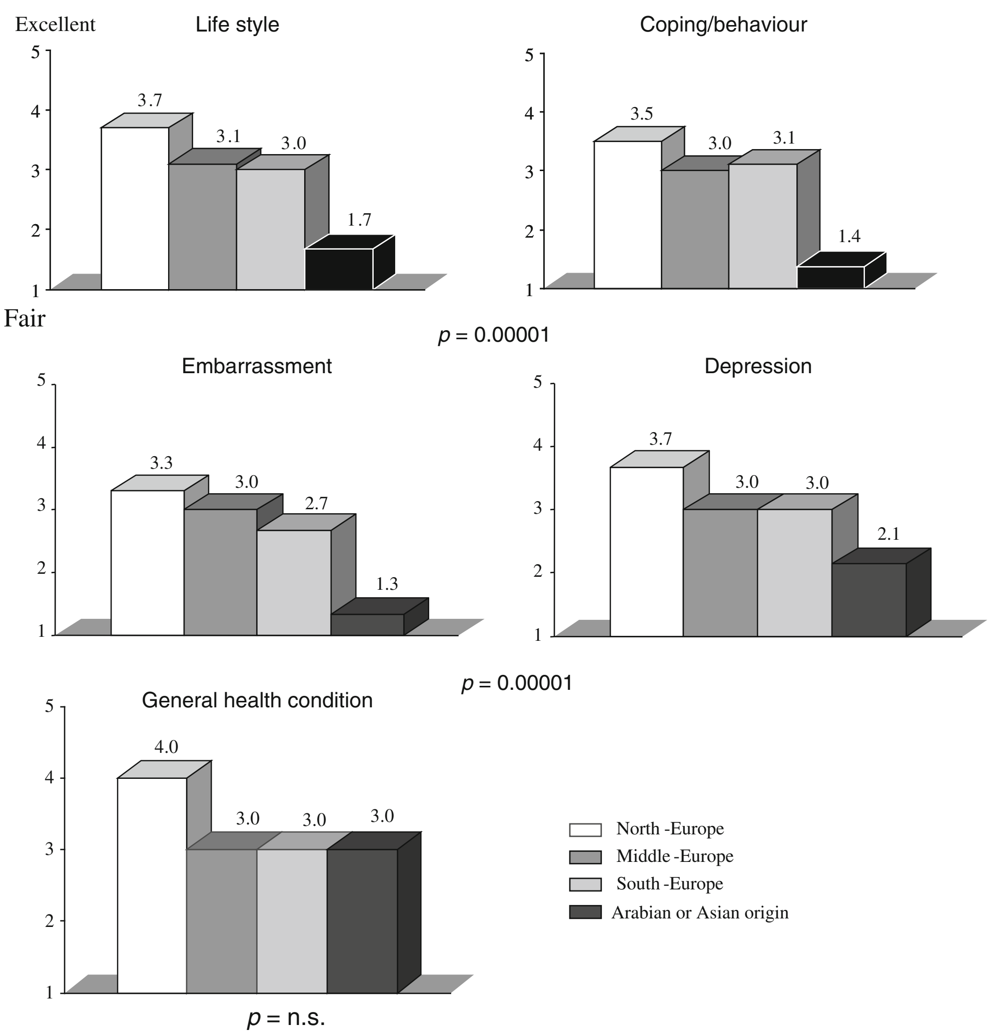

Fig. 1. Results of quality of life according to geographic origin

the formation of a permanent colostomy. Therefore, we tried to evaluate possible social and geographic factors which could have an impact on QOL of patients following APR: In a prospective trial patients operated on for low rectal cancer by APR were evaluated by a QOL questionnaire as mentioned above. The results for the four domains of QOL (Lifestyle, Coping behavior, Embarrassment, Depression), as well as for subjective general health were evaluated with regard to age, gender, education and geographic origin in an univariate and multivariate analysis (Table 2).

Thirteen institutions in 11 countries included data from 257 patients. While the analysis of results of general health did not reveal any significant differences, the analysis of the four domains of QOL showed a significant influence of geographic origin (Fig.1). The presence of a permanent colostomy showed a consistently negative impact on patients in southern Europe as well as in patients of Islamic origin. On the other hand, age, gender and educational status did not reveal a statistically significant influence [21].

There are many reasons for these statistically consistent findings in our study.

Since the worst QOL results in all domains were found in Muslim patients, we assume that religious factors may play a very important role. Kuzu et al. also described a significantly poorer outcome in patients following APR compared to patients with sphincter preserving surgery [22]. In the APR group, a significantly greater number of patients stopped praying daily and fasting during Ramadan. This resulted in significantly higher social isolation and affected QOL even more negatively.

Another aspect of the explanation for our findings may be attributed to the fact that post-surgical stoma care varies widely throughout Europe. It is obvious that patients who have standardized support available in hospital and (even more) at home, and who receive repeated counseling by qualified specialists in stoma care, will overcome daily problems arising from their colostomy much more easily than patients who are left alone in this situation. Furthermore, the presence of well-trained stoma therapists might also result in a higher percentage of patients using more sophisticated instruments like stoma irrigation, which leads to further improvement in QOL.

Furthermore, the constant and statistically-significant observation of the geographic influence in the various domains of quality of life proves that the situation after formation of a permanent colostomy is dependent on individual factors influenced by the social context and the patient's community. We feel that this observation could be taken into account when patients are given preoperative counseling. Furthermore, evaluations of QOL studies should also consider important aspects of the patient's life, such as social background, culture or religion.

Conclusion

QOL studies in oncology are of increasing importance. Their main aim is to determine the impact of cancer and its treatment on patients' well-being.

The availability of information on patient's preoperative expectation as well as existing data of postoperative QOL may help the surgeon before major surgery for rectal cancer.

The extreme form of sphincter preserving techniques leads to no significant reduction in most quality of life domains, only in the intestine specific domains.

The controversial results of quality of life outcomes after APR can be explained by different individual patient specific factors. As shown in our own studies, geographic and religious factors should be taken into account when QOL evaluations are considered [21]. A permanent stoma in southern Europe, in Muslim countries, probably also in Asia is viewed as a disaster.

In contrast, Renner et al. described quite good QOL results in patients with graciloplasty after APR [3].

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Do we need a pouch after intersphincteric resection?

Rudolf Schiessel

Introduction

In the early years of sphincter saving surgery for rectal cancer, an anorectal remnant of at least 6 cm seemed to be necessary for a satisfactory continence. Especially the sensory function of the lower rectum was assumed to be essential for a good postoperative function [1]. Gaston [2] has shown that after extensive resection of the rectum the rectoanal reflex was absent and continence was impaired. He showed on patients with rectal anastomoses in various levels that a minimum of 7 cm of rectal stump was necessary to elicit the rectoanal reflex, demonstrating an intact afferent and efferent nerve supply. His work showed very clearly that the lower rectum is an integral part of the sphincter mechanism. Although further clinical experience with different kinds of sphincter saving procedures did not confirm that a small rectal stump leads to incontinence, the important interaction between the lower rectum, the anal canal and the sphincter muscles is still valid.

Parks [3] reported 1982 his experience on 76 patients with coloanal anastomosis. Only one was incontinent out of 70 evaluable patients, the others were continent, but 30 had irregularities with 3 to 4 defaecations per day. The rectoanal reflex was absent in all cases [3]. With increasing experience with low rectal anastomoses, in particular after the widespread use of circular staplers, defaecation disorders, called the "anterior resection syndrome" were observed. This phenomenon was characterized by a high frequency of bowel movements, fractionated defaecations and urgency. Despite earlier observations incontinence was not the dominating problem. The assumption was an insufficient capacity of the neorectum. The awareness of these problems after anterior resection resulted in a study showing that patients with a permanent stoma after abdominoperineal resection had a better quality of life than patients after anterior resection [4, 5]. This was not confirmed by other studies.

In 1986 Lazorthes and Parc published their experience with the construction of a colonic pouch for establishing a reservoir after rectal excision [6, 7]. They used a J-shaped reservoir which was anastomosed to the anal canal. The complication rate was low and the postoperative function was good with 1–2 stools per day and no incontinence. Parc reported, that 25% of the patients had problems with evacuation, requiring enemas. In the following years a colonic J-pouch was used by many surgeons for reconstruction after anterior resection and ultralow resections as well. It became nearly a dogma to use a pouch. Numerous studies showed a functional advantage of the J-pouch over a straight colorectal or coloanal anastomosis. Most randomized studies found a better postoperative bowel function after a pouch. Although the data showed a reduced frequency of bowel movements in the first months after rectal surgery, it was not clear which criteria were necessary to justify a pouch construction. Many studies recommended a pouch after anterior resection, some after coloanal anastomosis. Parameters such as preoperative bowel function (constipation, diarrhea), sphincter function, bowel segment for reconstruction and the failure of pouch construction because of anatomical obstacles, were not studied sufficiently. Some studies used short follow up periods, therefore missing the important information, that patients without a pouch experience a steady improvement of their bowel habits 6 months after surgery or stoma closure. Thus in long-term studies the difference between patients with and without a colon pouch concerning stool frequency and incontinence episodes is not impressive. The construction of a colon pouch can be difficult or impossible in certain patients. Harris et al. [8] found in a study of 107 patients with coloanal anastomosis that in 28 cases a pouch construction was not possible. Major obstacles were a narrow pelvis, a bulky sphincter apparatus, diverticulosis and insufficient length of the colon. So the technical failure rate in this study was 22.4% with the J-pouch.

The high failure rate with the J-pouch stimulated the development of a simpler pouch by Zgraggen et al. [9]. This pouch consisted of a vertical incision of the colon that was closed in horizontal direction, similar to a pyloroplasty. This was called the transverse coloplasty pouch. Experimental and clinical data showed functional results equal to the J-pouch, but better than the straight anastomosis. Other data suggested that the reservoir volume was less important for neorectal function [10]. It was assumed that a short segment of reduced propulsive peristalsis was sufficient to improve the function of the neorectum. Huber [11] could show that a side to end anastomosis in low anterior resection had a similar outcome as a colonic pouch. Although the colon pouch was better in the early postoperative follow up, more evacuation problems were observed. The postoperative complication rate was statistically not different. In a later study by Machado [12] the equality of the side to end anastomosis was confirmed.

In order to resolve the controversial discussion concerning the preference of neorectal reconstruction after low stapled and coloanal anastomosis, a multicentre trial was conducted in order to compare straight anastomosis with J-pouch and coloplasty pouch. This trial included a total of 364 patients, the follow up was 2 years [13]. Included were patients with low rectal cancers and a coloanal anastomosis. Interestingly 96 patients were found to be ineligible for a J-pouch. This represents 26% of the total number of patients in this study. According to the protocol only the ineligible patients were randomized into a straight anastomosis and a coloplasty pouch. This resulted in a relatively small group with straight anastomosis (49 cases) and a low power for comparisons between the pouches and the straight anastomosis.

What did we learn from this excellent multicentre trial?

1. A J-pouch is in about 26% of the patients not feasible.
2. The J-pouch is superior to the coloplasty pouch with respect to the total number of daily bowel movements, pad usage, clustering and fecal incontinence score.
3. The quality of life is statistically not different between the pouch groups and the straight anastomosis.
4. At 24 months postoperatively bowel function is similar in the pouch groups and in the group with a straight anastomosis.

58% of the patients received a radiotherapy preoperatively, from these 51% additional chemotherapy. Under these circumstances and the assumption, that the patients with neoadjuvant treatment were evenly distributed, bowel function in all groups was surprisingly good. The trial confirmed earlier observations, that the J-pouch is only better than a straight anastomosis in the early postoperative period after a low rectal resection. But the differences are not really dramatic. Therefore the question arises if its really worthwile to construct a pouch under all circumstances. It is easy to construct a J-pouch in patients with a wide open pelvis, no obesity, a rectal stump of sufficient length, a long descending colon without diverticla and good blood supply. In the individual case it is sometimes very difficult to perform a safe pouch. In such cases it is better to avoid a pouch construction than to risk a postoperative complication. It should be never ratet as a mistake, when somebody did not perform a pouch after a low rectal resection.

The studies described above dealed with anterior resections with stapled anastomoses and low resections with coloanal anastomoses. For intersphincteric resections no comparative trial is available concerning colon pouches versus straight anastomosis. What makes the difference between ISR and other resections? The difference is the low level of the anastomosis in the anal canal, usually below the dentate line. At this level the side to end anstomosis with a J-pouch causes a lot of tension in the suture line, in particular when the anal canal is of considerable length. Another problem is the bulk of mesenterial fat that cannot be brought down to the lowest (and narrowest) part of the pelvis. It is therefore adviseable to perform a test-pull through before stapling a pouch, in order to check if the length of the colon is sufficient and the mesentrial fat is not squeezed by a narrow pelvis. Whenever the feasibility of a J-pouch is in doubt it should not be performed in order to avoid severe complications such as pouch necrosis or dehiscence of the coloanal anastomosis.

In case of the impossibility of performing a J-pouch we have 3 options:

1. A straight coloanal anastomosis
2. A coloplasty pouch
3. A myotomy of the colon used for pull-through (Fig. 1)

A straight coloanal anastomosis is still a good and safe option for reconstruction. We know from long-term studies, that problems such as a high stool frequency will improve within one year after the operation and the bowel function after 2 years will be equal to patients with a J-pouch.

Another option is a coloplasty pouch. This pouch can be used in patients with a narrow pelvis and in very low anastomoses and a long anal canal. Although this pouch does not increase the neorectal volume, it might help to reduce the frequency of bowel movements by interrupting the peristalsis of a hypermotile sigmoid. We have to take into account, that sometimes we are very limited in the availability of colon for neorectal reconstruction. Thus it can occur, that the available length of colon can only be achieved by using a part of the sigmoid with muscular hypertrophy and diverticula as well. In this case we can expect, that postoperative bowel function might be disturbed by a high frequency of defaecations and fragmen-

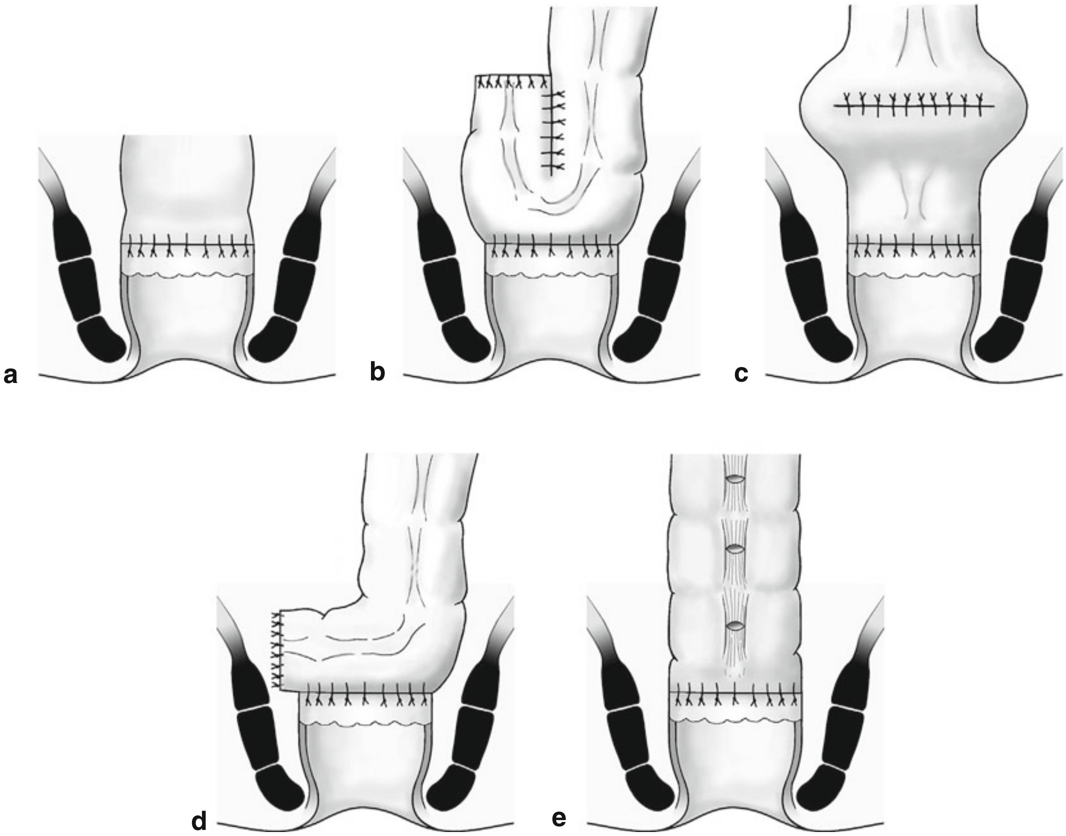

Fig. 1. Options for reconstruction after intersphincteric resection. (**a**) straight anastomosis, (**b**) J-pouch, (**c**) coloplasty pouch, (**d**) side-to end anastomosis, (**e**) taeniomyotomy

ted evacuations. In order to obviate this, a coloplasty pouch is an option as a second choice.

In a situation, where the length of the available colon is so limited that even a coloplasty pouch would be dangerous, we have used a taeniotomy as described by Hodgson [14] for diverticular disease. This method will also reduce the peristaltic activity of a sigmoid with muscular hypertrophy. We perform this myotomy on a length of 15 cm. It is easy to perform and does not reduce bowel length. Since we have used this method only in a few cases, it is difficult to give a clear recommendation based on solid data.

In general, the decision as to whether a pouch should be performed or not is more difficult in ISR than in other low rectal resections. This has to do with the lack of comparative trials and the very low level of the coloanal anastomosis. Whereas in "normal" low rectal resections in about one third of the patients the performance of a J-pouch is not possible, in our experience this goes up to 80% in ISR. Thus the decision has to be made by individual judgement depending on the local situation.

The determinig parameters are:

1. Length of the available colon
2. Mesocolic blood supply
3. Length of anal canal
4. Level of coloanal anastomosis
5. Volume of mesocolic fat
6. Diameter of pelvis
7. Muscular hypertrophy of colon
8. Diameter of colon
9. Preoperative sphincter function
10. Result of trial pull-through

Using these parameters a stepwise decision-making process can be used.

Factors favouring a pouch are:

1. Muscular hypertrophy of the descending colon or sigmoid.
2. Low sphincter pressures: resting pressure <50 mmHg, contraction pressure <50 mmHg.
3. History of frequent smooth stools.

Factors making a pouch less important are:

1. Normal colon with wide diameter.
2. Good sphincter function.
3. History with constipation.

In conclusion, the question: "Do we need a pouch after ISR?" is difficult to answer. We know, that a pouch can improve postoperative bowel function in the first postop-

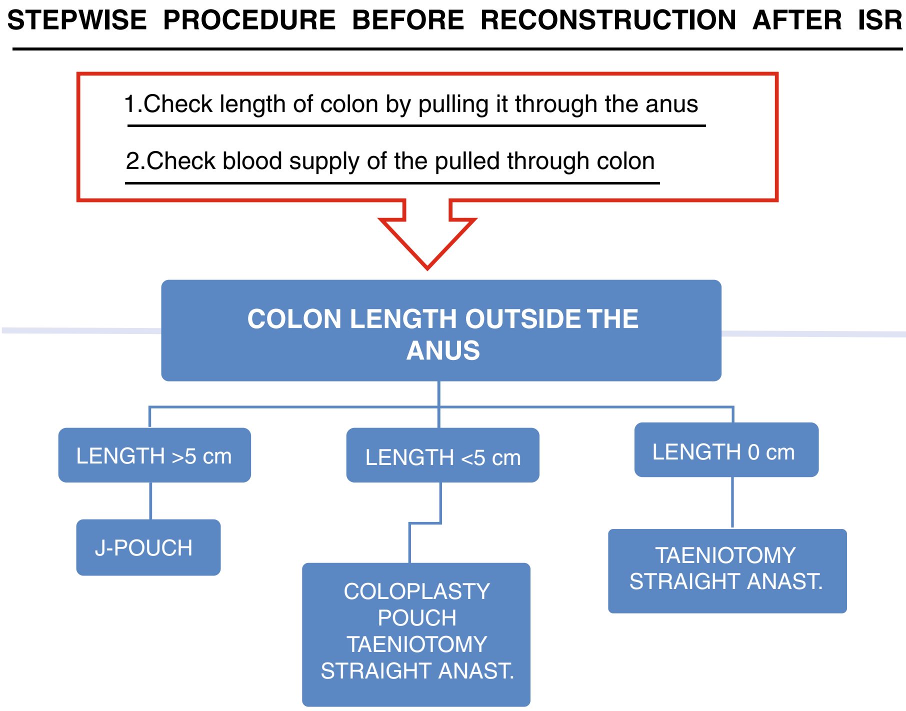

Fig. 2.

erative year, but in many cases it might be safer to use a simple coloanal anastomosis. There are many factors to be considered before a final decision is made.

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Management of limitations for sphincter preservation and functional failure following intersphincteric resection

Harald R. Rosen

Introduction

Oncological surgeons try to achieve the right balance between an acceptable oncological outcome and best possibly quality of life (QOL). The new definition of minimal safe margins as well as standardization of the surgical technique (with special emphasis on mesorectal excision) has led to the establishment of intersphincteric resection as an acceptable solution for ultra-low rectal tumors. The feasibility of this procedure has been repeatedly proven by our group as well as others in a considerable number of patients [1, 2]. Nevertheless, two limitations of the method must be taken into account:

(a) Oncological limitations
(b) Functional failure

In the following, we will focus on the above mentioned problems and describe therapeutic options to achieve better quality of life for patients undergoing this procedure.

Oncological limitations

The presence of a functionally intact external anal sphincter is an essential prerequisite to achieve satisfactory sphincter function after intersphincteric resection. Our observations as well as those of others have shown that direct invasion of low rectal tumors into the external anal sphincter is a rare event [3]. However, its occurrence is a mandatory indication for abdominal perineal excision (APE). Patients who present with extensive local tumor growth (either into adjacent organs and/or the external anal sphincter) will be candidates for a neoadjuvant treatment approach, including radiochemotherapy aimed at down-staging the tumor. A certain percentage of these patients will still have to undergo APE because of oncological considerations or functional problems of the anal sphincter following intensive radiotherapy. Once the decision to perform APE has been taken, **total anorectal reconstruction (TAR)** can be offered to the patient as a means of avoiding a permanent abdominal colostomy [4–6]. This method is based on two principles: the formation of a perineal colostomy and the construction of a "neosphincter" by the use of a skeletal muscle.

According to Lazorthes and coworkers, perineal colostomy was well accepted by some patients who would have otherwise had to undergo an abdominal colostomy and experience the poor quality of life associated with the procedure [7, 8].

The possibility of transforming skeletal muscle fibers by continuous low-frequency electrical stimulation into a muscle capable of tetanic contraction led to the introduction of electrodynamically stimulated graciloplasty. The procedure was first described by Baeten and Williams in the nineties of the last century [9, 10]. Briefly, the mobilized gracilis (or part of the gluteus) muscle is stimulated by electrodes which are applied to the most proximal neurovascular bundle. Conversion of the quality of muscle fiber is achieved over a "training period" of four to eight weeks during which the muscle is stimulated at a low frequency (5 Hz), which is gradually increased (16 to 21 Hz). This permits continuous contraction and closure of the "neoanal canal". Electrical stimulation is guaranteed by a subcutaneously implanted pulse generator (INTERSTIM, Medtronic Company, Kerkrade, Netherlands). The contracting muscle is relaxed and the anal canal opened by operating a remote control device which is in the possession of the patient (Figs. 1 and 2).

Our group as well as others have demonstrated the feasibility of this surgical approach for patients who had to undergo APE [4, 6]. Although total anorectal reconstruction is a technically demanding procedure associated with a considerable morbidity, a satisfactory outcome was

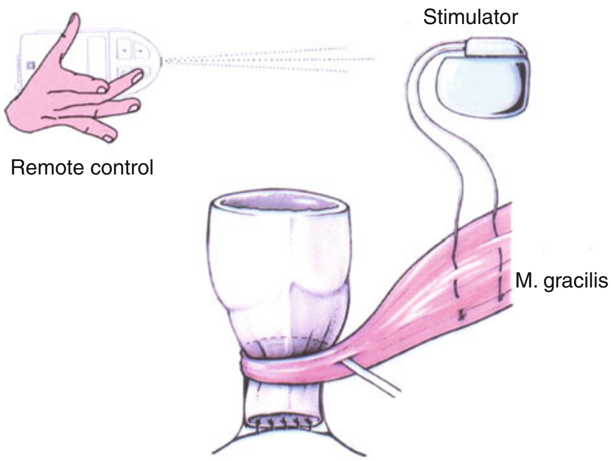

Fig. 1. The principle of the dynamic graciloplasty

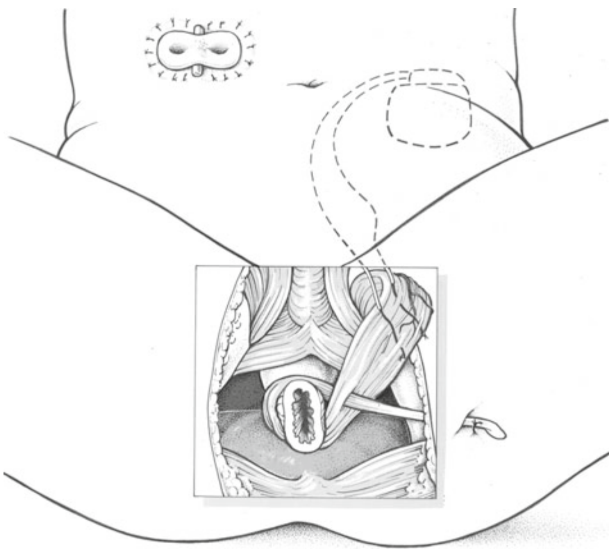

Fig. 2. Total anorectal reconstruction (TAR) with dynamic graciloplasty

observed in a considerable number of patients even in the long term [6].

Total anorectal reconstruction can be performed either in a single session after APE (**primary TAR**) or in patients who have undergone APE in the past (**secondary TAR**). Although the procedure is technically more demanding in the latter case, it provides a certain security with regard to local recurrence. It is usually performed only in those patients who have lived with a permanent colostomy and are convinced that they can no longer tolerate the situation. Therefore, this distinct but small group of patients will be highly motivated and will accept the potential morbidities as well as the functional problems associated with the procedure.

Alternatively to the use of gracilis muscle transposition the implantation of an artificial anal sphincter is

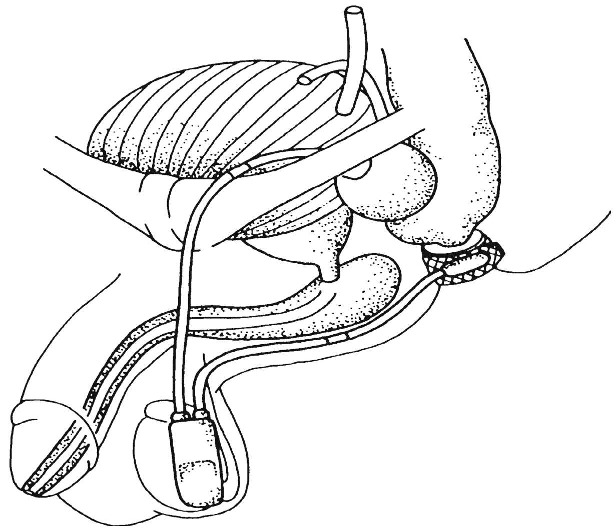

Fig. 3. Artificial bowel sphincter

a widely accepted method for sphincter replacement in patients suffering from severe faecal incontinence [11, 12]. However, with regards to the special indication of TAR there are only few reports in the literature dealing with this approach to create a "neosphincter" (Fig. 3). Not surprisingly, the infection rate is the most prominent problem due to the placement of a foreign body around the "neoanus". However, a few patients have been treated successfully with a secondary implantation following the creation of a perineal colostomy during APE [11, 12].

Although abdominal colostomy can be successfully avoided by TAR, certain functional limitations must be taken into account. The most prominent functional problems are defecation disorders, i.e. emptying problems. Cavina et al. as well as our group showed that, following TAR, irrigation of the neorectum is an important precondition to achieve satisfactory results [4, 6]. By application of an irrigation volume of 750 to 1500 ml of tap water every 24 to 48 hours, patients were able to achieve satisfactory 'pseudo'-continence. One may well ask whether an extensive procedure of this nature is justified as a substitute for the (much simpler) abdominal colostomy. It has been shown that a certain proportion of patients confronted with this situation will be candidates for it. Holzer et al. participated in an international multi-center trial to evaluate quality of life after APE, and showed that certain cultural and geographical conditions are responsible for a marked reduction in quality of life in patients who had undergone an abdominal colostomy [13]. The condition is especially irksome for patients who subscribe to the Islamic religion; this fact is ample evidence of the potential role of TAR in selected individuals.

Functional failure following intersphincteric resection

Change of bowel habits is a common and widespread problem after low anterior rectal resection. A number of patients undergoing resection of low rectal tumors with abdominal or coloanal anastomosis will have to pay the price for avoiding a permanent colostomy by accepting a combination of symptoms collectively known as the "anterior resection syndrome" [14, 15]. The lower the anastomotic line is situated, the greater is the patient's likelihood of developing functional disorders. The syndrome involves defecation difficulties with or without occasional incontinence and has been variously attributed to sphincter damage or denervation, the low level of the anastomosis, poor functioning of the "neo-rectum", as well as loss of rectal sensation. Recent experimental data suggest that surgical denervation of the left colon results in a significant increase in colonic motility, leading to repeated urgency and clustering of defecation, which are some of the most disturbing symptoms of the anterior resection syndrome [16]. Today it is widely accepted that more than 60% of patients undergoing low anterior resection will be confronted with severe functional problems which will markedly reduce their quality of life [15, 17]. The introduction of neo-adjuvant radiotherapy in the treatment regimen of low rectal cancer has further aggravated these functional problems [18, 19]. Pietsch et al. showed a significant reduction of resting and squeeze pressures, caused by innervation problems and fibrosis, in patients who had undergone low anterior resection [19].

Various approaches have been used to improve the functional outcome of low and ultra-low rectal resections. The creation of a new rectal reservoir by construction of a colonic J-pouch was shown to improve functional difficulties in the immediate postoperative period [17, 20]. However, this method as well as a side to end (Baker-type) anastomosis requires supra-anal location of the anastomosis in order to be technically feasible. A straight coloanal anastomosis with or without coloplasty will be the method of choice for a distinct subset of patients with specific anatomical limitations, who will be candidates for inter-sphincteric resection [2]. A certain number of patients will experience defecation disorders despite the presence of a good neo-reservoir and/or even after a longer follow-up (more than two years). Therefore, alternative approaches to overcome this partly debilitating condition were investigated, and have been published recently.

Sacral nerve modulation (SNM) is widely accepted as the method of choice for patients suffering from fecal incontinence. This method focuses on stimulation of the dorsal roots of the sacral nerves, thus achieving a modulation of afferent neural pathways from structures of the pelvic floor (bladder, rectum, pelvic floor muscles) to the central nervous system. In general this therapy consists of three steps which are an acute needle test during which the efficacy of the sacral nerves is tested by external stimulation. If successful this is followed by a trial period of 2–3 weeks during which the patients stimulates the nerve with a portable external stimulator) percutaneous nerve evaluation – PNE). If a functional improvement can be achieved the whole system (nerve electrode + stimulation generator) can be implanted permanently (Fig. 4).

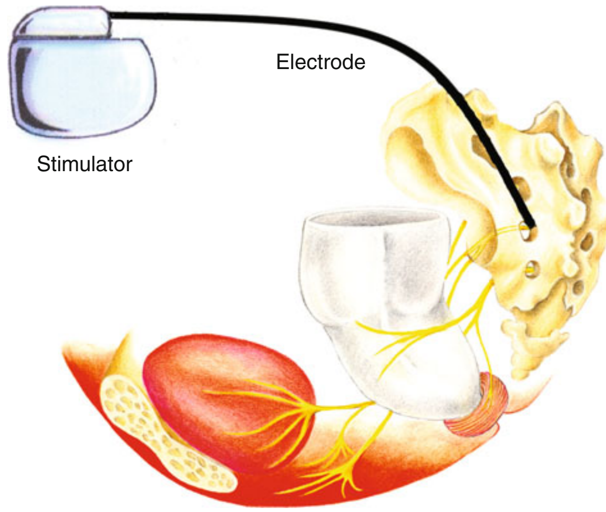

Fig. 4. Principle of sacral nerve stimulation with permanent implantation of a sacral lead ("tined lead") and a pulse generator

Some groups have tried to use this technique in a small number of patients suffering from the anterior resection syndrome [21, 22]. After the first successful case reports, the authors of recent publications (still comprising small patient numbers) have reported promising results and positive changes in neo-rectal parameters following SNM [22]. Although the postulated mechanism of this procedure is largely speculative in nature, SNM does appear to exert a beneficial effect in patients who have experienced neurogenic injuries following radiotherapy or rectal resection. Therefore, it would be appropriate to consider this procedure in a selected number of patients.

Another approach consists of voluntary emptying of the neorectum by means of transanal irrigation (TAI). This method has been repeatedly applied in pediatric patients (for incontinence following surgery for anal atresia) as well as in patients suffering from incontinence due to spina bifida or other neurologic disorders [23]. Iwama et al. described the use of TAI for patients with defaecation disorders following rectal resection for the first time

Fig. 5. The Peristeen-system for transanal irrigation (TAI)

in 1989 [24]. However, this cheap and easily feasible treatment failed to gain the necessary acceptance.

With the introduction of more and more user friendly devices some authors recently focused on the use of TAI for patients with faecal incontinence as well as with constipation [25, 26].

Based on our experiences with TAI in patients following TAR (as mentioned above) we included patients suffering from anterior resection syndrome (i.e. multiple defaecation episodes during day and night, clustering of bowel motions with or without incontinence) who showed a minimum history following rectal resection of nine months into a prospective, two centre (Vienna, Geneva) study. Patients were trained by specialized stoma nurses to perform TAI by use of the Peristeen(r) system (Coloplast A/S, Humblebaek, Denmark) (Fig. 5).

After a median follow-up of 29 months (15–46 months) 14 patients emptied their bowel with a median volume of 900 ml (500–1500 ml) of tap water every 24–48 hours. Incontinence scoring, QOL domains of the ASCRS questionnaire for incontinence as well as the mental component of the SF-36 questionnaire improved significantly following application of TAI in these patients who had failed to improve by other treatment options (Rosen et al., Colorectal Disease, in press).

In conclusion, the occurrence of rectal emptying disorders following low anterior or intersphincteric resection has to be taken into account in the immediate postoperative course but also in the long term. Patients need to be informed about this situation as well as the therapeutic possibilities which are available to overcome these problems. Together with this, intersphincteric resection or total anorectal reconstruction are successful methods to help patients to avoid the formation of a permanent abdominal colostomy.

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About the editors

Rudolf Schiessel started his academic career in the University Clinic of Surgery of Vienna Medical School. His surgical training comprised in addition to general surgery, traumatology, urology, thoracic surgery, experimental surgery, vascular surgery, gastroenterology and intensive care.

An important step in his career was his training with John Goligher in the Leeds General Infirmary, where he learned new methods in colorectal surgery, patient evaluation and scientific methods as well.

Another step was his work with William Silen at Harvard in Boston. In his laboratory he studied the protective mechanisms of gastrointestinal epithelia. After returning to Vienna he established a research laboratory with cooperations with Beth Israel Hospital and Tufts University in Boston. His surgical career focused more and more on colorectal surgery. 1984 the first patient with a low rectal cancer was operated with an intersphincteric resection. The first results were encouraging: no complications, continence surprisingly good. But it was a long way to go. In order to proof the oncological and functional safety of this technique many patients had to be observed over a long time. 1994 he published his first series in the British Journal of Surgery. He could show that this operation was an alternative to APR in selected cases and that the resection of the internal sphincter did not cause fecal incontinence. In 2005, he could report a larger series with a median follow-up of 6 years and a local recurrence rate of 5.3% showing its oncological safety.

1992 he became chief of the Surgical Department of Donauspital in Vienna, a new and very modern teaching hospital. Here he founded the Ludwig Boltzmann Institute of Surgical Oncology, devoted to research in sphincter salvage and sphincter restoration in rectal cancer. He was president of the World Congress of Coloproctology in 1998 in Vienna, President of the Austrian Society of Surgery and the Austrian Society of Coloproctology. He has published 262 original papers with publications in Nature, Am. J. Physiology, Cancer, GUT, Gastroenterology, Brit. J. Surg., J. Clin. Invest., J. Clin. Oncol., and Dis. Colon Rectum. He has written 22 book chapters. He achieved several awards such as Billroth-price, Honorary Medal of Polish Society of Physiology and Central European Price for Innovative Cancer Treatment. He was visiting professor at Georgetown University Washington and Universities in Seoul, Teheran, Bagdad and Tripolis.

His vision for the future: no patient with rectal cancer should need a permanent stoma.

Peter Metzger started his academic career at the 3rd Surgical Department of the Semmelweis Medical University in Budapest. After focusing on visceral surgery, his training comprised of thoracic surgery, traumatology, vascular surgery as well as intensive care medicine. A significant step in his career was his work with Franz Paul Gall, Paul Hermanek, Werner Hohenberger, Johannes Scheele, and Hubert Zirngibl in Erlangen from 1986 to 87. His main focus was on sphincter saving surgery of very low rectal carcinoma. He learned the "Erlanger technique" of the Whipple operations by Franz P. Gall. After returning to Budapest, he established this new sphincter saving surgical technique at the 1st Surgical Department of the Postgraduate Medical University. In 1991, he became the first surgeon in Hungary to establish laparoscopic rectum resections and three years later he published his first results in a book written by Steven Wexner. In 1994, together with his colleagues Gamal E. Mohamed and János Kiss, he founded the Hungarian Society of Endoscopic Surgery. He was appointed second chief at the Surgical Department of the University of Regensburg because of his achievements in laparoscopic colorectal surgery.

He was promoted chief of the Teaching Hospital of the Semmelweis Medical University in Budapest with his focus on extended laparoscopic oncological surgery. In 1998, he worked in Germany with Hubert Zirngibl, who had the same interest and enthusiasm as second chief at the Witten-Herdecke University.

Since 1998, he has been continuing his surgical career in Vienna, Austria, and has developed a special technique for laparoscopic intersphincteric resection for very low rectal cancer together with Rudolf Schiessel.