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ČASOPIS ČESKÉ ONKOLOGICKÉ SPOLEČNOSTI A SLOVENSKEJ ONKOLOGICKEJ SPOLOČNOSTI

THE JOURNAL OF THE CZECH AND SLOVAK ONCOLOGICAL SOCIETIES

EDITORIAL

Dear colleagues,

it is a great honour and privilegefor me to welcome you at the 5th Central European Congress of Coloproctology and Viscerosynthesis here in Brno.. At this occasion, let me present you several selected lectures, which are to be presented at this meeting. The topics concern the most Apopular topics in malignant coloproctologic diseases: colon and rectal carcinoma (because of its frequency) and anal carcinoma (because of its low incidence and therefore difficult treatment). The prominent authors are both national and international, wellknown leading authorities. We are really proud to be allowed to present their points of view in so very important fields of coloproctology and viscerosynthesis. We are really glad that by means of this extra issue of Archives of Oncology (Klinická onkologie), this knowledge could be spread in so many countries, especially of so called "Eastern Europe".

Traditionally, people not only from Central Europe, but from other continents, too, meet here to exchange their knowledge, opinions and start friendly relations.

Our aim of the Congress and of this special issue is to compare the present state of knowledge of the most important fields in coloproctology, concerning the malignant diseases, i.e. colorectal carcinoma and anal carcinoma, including diagnosis, prognosis, adjuvant and surgical treatment. It should be help to our colleagues not only in our country, but in other countries, too.For this reason, the invited lectures are strictly practical. However, it is desirable that all physicians and surgeons dealing with coloproctology should have an understanding of our present knowledge of other aspects of these diseases, so contributions dealing with such a topics as precanceroses and new technologies are included.

We have been fortunate enough to assemble a distinguished international team of contributors and it is a great plesure to have this opportunity to thank them.

I would like to take the opportunity here to thank all those who worked so hard in the preparation of this meeting and all our sponsors who made this event possible. The most important is, however, Your particular contribution with scientific reports and discussions during the sessions. We hope that our joint efforts will result in a succesful meting in the benefit of our patients with colorectal diseases.

We also thank the publishing staff of Klinická onkologie for their cooperation. They have given us practical assistance, for which we are grateful, and we especially thank to their executives, with them it has been pleasure to work.

Vážené kolegyně a kolegové,

je pro mne velkou poctou přivítat Vás zde v Brně na 5. středoevropském kongresu koloproktologie a viscerosyntézy. Kde se tradičně setkávají lidé nejen ze střední Evropy, ale i z jiných světadílů, vyměňují si své znalosti, názory a přátelí se. Dovolujeme si při té příležitosti prezentovat několik vybraných přednášek, které zde zazní. Tématem jsou „nejpopulárnější" témata maligních koloproktologických onemocnění: karcinom rekta a kolon (pro svou častost) a análního karcinom (pro svou nečetnost a tím obtížné léčení). Autoři jsou známé kapacity jak na národní, tak na mezinárodní úrovni. Jsme hrdi na to, že můžeme publikovat jejich názory v takto důležitých oblastech koloproktologie a viscerosyntézy.

Současně jsme velmi rádi, že možností vydat je jako zvláštní číslo Klinické onkologie můžeme tyto poznatky dále šířit, především v takzvané „východní Evropě".

Snahou kongresu i tohoto zvláštního čísla je srovnat stav vědomostí v nedůležitějších oblastech koloproktologie, zabývajících se maligními onemocněními, tj. kolorektálním karcinomem a análním karcinomem, včetně diagnostiky, prognózy, chirurgické a adjuvantní léčby a tím pomoci kolegům jak v naší zemi, tak zemích dalších. Z toho důvodu jsou vyžádané přednášky přísně praktické. Vzhledem k tomu, že je nutné, aby všichni lékaři, zabývající se koloproktologií, měli přehled o současných vědomostech i v jiných aspektech těchto chorob, zahrnujeme i témata jako jsou prekancerózy, nové technologie a komplikace.

Využívám této příležitosti, abych poděkoval všem, kteří svou prací zajistili přípravy tohoto setkání a všem našim sponzorům, kteří setkání umožnili. Nejdůležitější je však Váš přínos v podobě přednášek, posterů a diskuse. Doufáme, že toto setkání bude úspěšné a přínosné pro naše pacienty s kolorektálními onemocněními.

Děkujeme také redakční radě Klinické onkologie za jejich spolupráci, za praktickou pomoc a především chceme poděkovat výkonné radě, s níž bylo potěšení pracovat.

General Secretary of 5th Central Congress of Coloproctology
President of the Czech Section Coloproctology

Hlavní tajemník 5. středoevropského kongresu koloproktologie a viscerosyntézy
Předseda Koloproktologické sekce ČCHS

Tomáš Skřička

5th Central European Congress of Coloproctology and Viscerosynthesis.

SELECTED LECTURES

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VYBRANÉ PŘEDNÁŠKY

OBSAH

ANAL CANCER

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The understanding and treatment of anal cancer has undergone a major changes. Twenty years ago, radical surgery in the form of abdominoperineal resection was the only possibility for cure. Combined modality treatment with irradiation and chemotherapy has resulted in increased survival and in sphincter preservation for most patients (1-7).

ANATOMY

The anal canal is about 3 cm to 4 cm long and extends from the anal verge to the level of the pelvic floor. The superior margin is determined clinically by the palpable upper border of the anal sphincter and puborectalis muscle as anorectal ring. The distal end of the canal at the anal verge can be defined as palpable groove between the lower edge of the internal sphincter and subcutaneous part of the external sphincter (8). The American Joint Committee on Clinical Staging and the Union Internationale Contre le Cancer (UICC) (9) recommend this definition of anal canal, rather than a convention used by some centers under which carcinomas that arise above or exactly at the dentate line are classified as anal canal tumors and those lying mainly or entirely below that line are called anal margin tumors (10-15). Perianal carcinomas are arbitrarily considered to be cancers arising from the skin within a 5 cm to 6 cm radius of the anal verge. This distinction is an important one, because squamous or basal cell cancers below the anal verge (perianal cancers) are skin cancers from a biologic and therapeutic perspective.

Four different types of epithelium are found within the anal region (8). The perianal skin is similar to hair-bearing skin elsewhere and contains many apocrine glands. At the anal verge, the skin become with a zone lined by modified squamous epithelium, which lacks hair or glandular structures. This squamous zone merges just below the dentate line (also called the pectinate line), which marks the line of the anal valves, with a transitional epithelium that incorporates features of rectal, urothelial, and squamous epithelia. The transitional zone extends proximally for about 20 mm until rectal mucosa becomes dominant.

PATHOLOGIC CLASSIFICATION

Epidermoid carcinomas now can be classified as squamous, basaloid or mucoepidermois tumors.

Squamous Cell Carcinomas may be keratinizing or nonkeratinizing. The well-differentiated type tend to arise from the skin of the anal margin, whereas the poorly differentiated tumours occur more frequently within the anal canal. According to Morson (16), more than 80% of tumors of the margin produce keratin whereas only 50% of tumors in the anal canal do so.

Basaloid Tumors arises from the cells of the anal transitional zone (17) and are also known as cloacogenic or transitional tumors18. They account for 30-50% of all anal canal cancers (19,20,21). These tumors may resemble carcinomas of anoepithelium or they may have patterns similar to basal cell carcinoma of the skin.

Mucoepidermois Tumors are rare. They occur in the anal canal and consist of squamous cells that produce both mucus and keratin (22). A careful search using mucin stains may find of mucinproducing cells in approximately 10-15% of patients with epidermoid cancers (23). These tumors behave in the same way as all other squamous cell carcinomas of the anus.

SPREAD

Direct spread of anal squamous cell carcinoma is preferentially in an upwards direction into the lower rectum. The reason is said to be because the line of least resistance is upwards in the submucous layer (24). Lymphatic spread commonly occurs to the inguinal nodes, but it is often not appreciated that spread to the superior haemorrhoidal lymph nodes and the nodes on the lateral wall of the pelvis is as common.

There is a relationship between the degree of histological differentiation and the incidence of lymph node metastases (12) since well-differentiated lesions rarely spread to the nodes. Although such a statement seems reasonable, in the absence of detailed microscopic examination of the inguinal nodes there are insufficient data to confirm this suggestion. Squamous cell carcinoma of the anal margin spreads in a way similar to skin carcinoma, with direct spread deep to the dermis. Lymphatic spread to the inguinal nodes is said to occur in 40% of cases (24).

Mesenteric lymph nodes are involved in one third to one half of patients with anal canal cancers treated by abdominoperineal resection (10,15,25-28). The risk of mesenteric lymph node spread from anal margin cancers is less defined. Patients treated by abdominoperineal resection, mesenteric lymph node spread was identical to that in patients with anal canal cancers (10,26), however, other two series, the risk was almost zero (25,29). Because the cure rate from local excision alone with anal margin cancers less than 5 cm in diameter is 90%, it appears that spread to mesenteric lymph nodes is infrequent, except in cases of massive disease (30). In a series of 45 patients with anal cancer (primarily of the anal canal) treated at Memorial Sloan-Kettering Cancer Center with a surgical procedure that included excision of the obturator and hypogastric nodes, pelvic node metastases were found in one third (27). However, case selection for such extensive surgery and pathology may result in overestimation of the risk of pelvic node spread.

The inguinal and external iliac nodes are the regional lymphatics considered in the T N M staging system. Patients may present with synchronous or metachronous inguinal lymph node metastases. Inguinal node metastases are extremely rare for T1 tumors or if the surface area of the primary tumors less than 4 cm (2,10,31). The overall risk of inguinal node metastases approximately 30% (10,12,27). Hematogenous metastases occur in few patients. Because of the dual venous drainage of the area, metastases occur equally to the liver and lung (32).

DIAGNOSIS

Because the initial symptoms of anal cancer are similar to those of common benign anorectal conditions, the patient often delays seeking the diagnosis. Because anal cancer is rare and examination may be painful and difficult if spasm occurs, physician related delays also occurs. Almost one third of the patients even at the Cancer centers with squamous cell cancer of the anorectum were thought to have had benign disease until biopsies proved otherwise (27). More than half of the patients in the Mayo Clinic study had associated benign anal abnormalities, such as fistula in ano, fissure or hemorrhoids (33).

Bleeding, pain, and a sensation of a mass are the most common symptoms. Pruritus is less frequent, except in patients with perianal cancer (33). Physical examination should include digital anorectal examination, anoscopy and proctoscopy, and palpation of the inguinal lymph nodes. Associated Bowen's or Paget's disease of the perianal skin increase the likelihood of anal carcinoma. The differential diagnosis for bleeding, pain, or a mass sensation includes

thrombosed hemorrhoid, fissure, fistula, perianal or crypt abscess, benign anal papiloma, and adenocarcinoma of the rectum. Patients with severe pain and spasm may be treated empirically with analgesics, stool softeners, warm baths, and topical ointments for 1 to 2 weeks. Persistent symptoms may require examination under sedation or general anesthesia to avoid missing the diagnosis of cancer or an inadequately treated infection.

Biopsy is necessary to confirm the diagnosis. Excision should not be attempted, except for superficial lesions detected very early. Suspicious inguinal lymph nodes should be biopsied to differentiate inflammatory from metastatic lymphadenopathy. Formal groin dissection should be avoided. Needle aspiration of the groin nodes for cytology may be attempted first. It the results are negative, surgical biopsy should follow.

In addition to physical examination and surgical staging of a suspicious inguinal node site, staging includes chest radiography and ultrasonography tests. Computed tomography (CT) and intraanal sonography have been suggested as useful tools in evaluating primary anal tumors (34,35). Marker studies have not been clinically useful, but a squamous cell carcinoma antigen can be monitored in serum and can reflect tumor status in some patients (36).

STAGING

Staging of anal carcinoma is difficult. Duke's stages cannot be applied as the tumor spreads to inguinal and iliac nodes which are not routinely removed at operation. The T N M system has been applied, but it can be criticized since it is difficult to distinguish tumors limited to the internal sphincter (T1) from those that involve the external sphincter (T2), and because extension into the rectum or perianal skin (T3) does not necessarily indicate a poor outcome (37). Numerous modifications of the T N M system have been tried (19,20,37-39) but none has proved acceptable. There have been few attempts to stage margin tumors. Staging system is recommended by the International Union Against Cancer. Definition of anatomical regions is made where anal canal is divided into 3 parts and into 3 parts of circumference, describing primary tumor (T) of anal canal:

Tis pre-invasive carcinoma (carcinoma in situ).
TO No evidence of primary tumor.
T1 Tumor occupying not more than one third of the circumference or length of the anal canal and not infiltrating the external sphincter muscle.
T2 Tumor occupying more than one third of the circumference or length of the anal canal or tumor infiltrating the external sphincter muscle.
T3 Tumor with extension to rectum or skin but not to other neighboring structures.
T4 Tumor with extension to other neighboring structures.
TX The minimum requirements to assess the primary tumor cannot be met.

Primary tumor (T) of the anal margin are described as follows:
Tis pre-invasive carcinoma (carcinoma in situ).
TO No evidence of primary tumor.
T1 Tumor 2 cm or less in its greatest dimension strictly superficial or exophytic.
T2 Tumor more than 2 cm but not more than 5 cm in its greatest dimension or tumor with minimal infiltration of the dermis.
T3 Tumor more than 5 cm in its greatest dimension or with deep infiltration of the dermis.
T4 Tumor with extension to muscle and bone, etc.
TX The minimum requirements to assess the primary tumor cannot be met.

Regional lymph nodes of anal canal are the perirectal nodes and nodes distal to the origin of the inferior mesenteric artery, where
NO No evidence of regional lymph node involvement.
N1 Evidence of involvement of regional lymph nodes.
NX The minimum requirements to assess the regional lymph nodes cannot be met.

Regional lymph nodes of anal margin are inguinal lymph nodes and are classified as follows:
NO No evidence of lymph node involvement.
N1 Evidence of involvement of movable unilateral regional lymph nodes.
N2 Evidence of involvement of movable regional lymph nodes.
N3 Evidence of involvement of fixed regional lymph nodes.
NX The minimum requirements to assess the regional lymph nodes cannot be met.

TREATMENT

There are some differences in management of the anal margin and anal canal carcinoma in regard of local or extensive surgery, irradiation or chemotherapy modes.

ANAL MARGIN CARCINOMA

Local surgery

Superficial perianal skin carcinomas (i.e., squamous and basal cell) outside the anal verge may be treated with wide local excision with good results. Excision with 1 cm margins, using primary closure, is usually appropriate. A skin graft can be placed if the surgical defect is large. Rarely are formal skin flaps necessary or desirable. A split-thickness skin graft will shrink with time, leaving a relatively small defect that will not interfere with the defection of local recurrence.

Multiple biopsies from the margins are crucial (40,41). For early noninvasive lesions, oral retinoids have been successful (42). Primary abdominoperineal resection is almost never indicated as the initial treatment of anal margin lesions. The cure rate after local excision for superficial squamous cell tumors exceeds 80% (12,16,30,33,43).

Local failure rates are higher if the anal margin cancers includes tumors in the anal canal distal to (not involving) the dentate line. (30) In Memorial Sloan-Kettering Cancer Center experience, disease recurred locally in 9 of 31 pateints treated with local excision for anal margin cancers. (30) Eight of these tumors were amenable to second local excisions.

Deeply infiltrative anal canal margin carcinomas have been treated with abdominoperineal resection. (10,30) Although most patients were cured, the small number of reported cases of disease defined as anal margin cancers does not allows detailed analysis of end results. Patients with invasive Paget's disease or with an underlying associated anorectal carcinoma usually require abdominoperineal resection with wide excision of the perianal skin.

External Irradiation

Epidermoid carcinoma of the anal margin tends to be early or only moderately advanced at the time of diagnosis, with lymph nodes only rarely involved (0-15%), usually in larger tumors 9 (5 cm in diameter). (39,44-46) Although these early cancers of the anal margin are successfully treated by local excision, radiation therapy should be considered for some patients. Papillon suggested that radiation therapy should be used for patients with anal margin carcinoma that is considered unresectable or patients who have extensive or recurrent lesions, patients who are medically inoperable can have radiation therapy.

Although some early studies of anal margin irradiation used interstitial radium needle implants, the high incidence of radionecrosis and uncontrolled irradiation fields indicated that external-beam radiation therapy was a better modality. (44,84) Although photons are most frequently used for these treatments, electron-beam therapy may also be successfully used for early perianal epidermoid carcinomas. (47) Results of treating perianal lesions, stage for stage, are similar to results for anal canal lesions; more extensive lesions require more aggressive therapy. (45,48) Although some researches recommended abdominoperineal resections for extensive lesions, radiation therapy appears to be an excellent alternative that yields cures with sphincter preservation. (45)

Most patients with anal margin tumors can be treated with excision alone, or with irradiation alone for more advanced or recurrent tumors. Concurrent irradiation and chemotherapy is an interesting but still investigational approach to advanced margin tumors.

ANAL CANAL CARCINOMA

Local disease

None of 10 patients initially treated at the Cleveland Clinic by local excision experienced recurrence of the disease. (49) Included were cancers of the anal margin and anal canal that extended less than one half the circumference; cancers involving the dentate line were excluded. Internal or full thickness sphincter excision with skin-graft coverage resulted in acceptable continence. In a review from the Connecticut Cancer Registry reported by Kuehn and colleagues, 26 patients with anal cancer, including distal and canal cancers, were treated by local excision, and 20 (77%) were cured. (50)

Trie Mayo Clinic experience with anal cancers between the dentate line and the anal verge includes 19 patients treated by local excision. (51) Treatment failed locally in 1 of 12 superficial tumors, which was subsequently cured with abdominoperineal resection. Seven patients with underlying sphincter muscle invasion refused radical surgery and were treated by wide local excision, some with adjuvant irradiation. Disease recurred locally in 3. (51) In a group of 5 patients (4 with Tl disease) treated at the Lahey Clinic by local excision, none had disease recurrence. (52) Of 144 patients treated at Memorial Sloan-Kettering Cancer Center for anal canal cancers (dentate line involvement), only 11 were suitable candidates for local excision. The 5-years survival rate was only 45% and most had local recurrence. (53)

Locoregional Disease

Multimodality therapy. Because integrated multimodality therapy improves overall survival and allows radical surgery to be avoided for most patients, the scope of initial diagnostic surgery should be limited to maximize the final functional result.

For anal margin cancers distal to the anal verge, a punch or surgical incisional biopsy performed in the office can suffice. For patients with considerable spasm and pain, examination and incisional biopsy under general anesthesia is appropriate. If a decision is made to proceed with local excision only (i.e., small anal margin or Tl anal canal lesion), the bowel is prepared, and elective surgery is performed.

Grossly positive inguinal lymph nodes are studied initially by needle aspiration cytology; open biopsy is performed if the specimen is benign. Minimally suspicious nodes warrant an excisional biopsy of one or two lymph nodes, using great care to avoid a hematoma or lymphatic leak. A superficial groin dissection is not necessary or useful as part of the initial treatment strategy. It delays definitive chemotherapy and radiation treatment, and it may increase the risk of leg edema after combined treatment.

Chemotherapy and radiation. In the past 20 years, increasing evidence from single-arm studies indicates that initial chemotherapy plus radiation therapy yields a very high rate of tumor regression, including a high rate of complete remission, and that surgery may not be required for many patients, or it may be limited to an excisional biopsy of residual scar. Even patients with relatively large anal epidermoid tumors may be spared a colostomy and have an excellent survival expectation.

Table 1 summarizes the results of therapy from several large series. (6,54-63) There are also results from prospective controlled randomized trials comparing multimodality therapy with irradiation alone or surgery alone. One retrospective study suggested a higher cure rate with multimodality therapy in patients with higher-stage disease. (64) Because conducted trials have been so impressive, with only modest morbidity, chemotherapy plus irradiation has been accepted as conventional treatment for most patients with anal canal disease. Some investigators still favor irradiation alone, but few support abdominoperneal resection as first line therapy.

The series in Table 1 followed a chemotherapy protocol similar to that pioneered by Nigro and coworkers. 5-FU was given by continuous 24-hours infusion for 4 to 5 days with a single bolus dose of mitomycin-C. (65) Combined therapy has been given concurrently or sequentially. In the concurrent regimen, radiation therapy and chemotherapy are initiated on the same day. In the sequential regimen, chemotherapy is given before radiation therapy. In addition to differences in timing of administration, the dose of radiation therapy has also varied (see Table 1). In some centers chemotherapy plus radiation therapy has been given before a planned surgical procedure - initially abdominoperineal resection and later local excision. Others planed radiation therapy to higher total doses as definitive treatment, but surgery was not part of the treatment plan. Despite these differences between trials, there is little evidence from these studies that one schedule or dose level is markedly superior to another. Response and survival rates are similar, although fewer patients require an abdominoperineal resection after concurrent chemotherapy and radiation therapy to higher doses.

Long-term follow-up results are becoming available. These reports give a reasonable picture of the number of patients eventually requiring abdominoperineal resection and of the number of patients in whom anal continence remained for a long period after nonoperative treatment with radiation therapy and chemotherapy. For example, Tanum and colleagues reviewed the experience in 106 Norwegian patients who received radiation plus concurrent mitomycin and 5-FU. (61) The radiation dose was 50 Gy given in 2-Gy fractions to most patients by anteroposterior and posteroanterior (AP/PA) parallel opposed fields. The complete response rate to chemotherapy was 84%; 16% of patients (i.e., positive biopsy) underwent abdominoperineal resection. Of 89 patients who were followed for a minimum of 3 months after treatment, 14 (16%) had significant morbidity within 2 years of treatment, which eventually required surgery or seriously impaired normal social life. Similar data with 87% 5 years survival rate is reported by D.Beck. (7)

When chemotherapy and irradiation are combined, AP/PA pelvic fields should probably not be treated to a dose higher than 40 Gy. Most investigators coned down to the primary site after 30 Gy. Miller and colleagues reported the results of 42 patients who received mitomycin and 5-FU followed by irradiation beginning 1 week after chemotherapy. (56) Twenty-three patients were initially treated with wide local excision. Two underwent abdominoperineal resection soon after local excision because of persistent cancer. Of 21 remaining patients, 3 patients later had abdominoperineal resections. Eighteen patients retained anal continence.

Some investigators found that any patient with a positive biopsy after initial treatment was certain to have recurrence of disease, (66) however, others has had long-term disease-free survival despite residual disease after induction therapy. (56,67,68) Of 44 patients in the original series, 18 (41%) had positive pathologic results after chemotherapy followed by irradiation. (67) At least half of these patients had no recurrent tumor detected at their most recent examinations.

Nigro made the point that combined therapy using chemotherapy plus irradiation can safely be given in a community setting 69 and it was supported by others studies. (59,60,70,71)

The best chemoradiation therapy regimen and the most appropriate radiation dose to use for patients with anal canal tumors limited to the primary site have not yet been defined. Distant failure is not the major problem. Local recurrence is more common, especially if the radiation dose is low (30Gy). 5-FU is probably a radiosensitizer, although there is some disagreement, but mitomycin is probably not synergistic. (72-74) Byfield and coworkers treated 11 patients with a 120 -hours infusion of 5-FU (25mg/kg/day) and concurrent irradiation, omitting mitomycin. (75) Radiation therapy was given in 4-day cycles (10Gy/cycle), separated by at least 9 days, to a total dose of 30 Gy to 47.5 Gy. All patients had complete clinical regressions; only 1 patient had active disease histologically. There was only a single local recurrence.

Table 1. Results of Multímodality Therapy for Anal Canal Carcinoma

Investigations	Chemotherapy Regimen	Radiation Therapy Regimen	Patients Evaluable	Abdominoperineal Resection Performed	Treatment Related Deaths	5-Years Survival (%)
Wayne State (55)	5-Fu: 1000 mg/m^2/4 days 2 cycles* Mito: 15 mg/m^2 d 1	30 Gy/15 fx	104	31	0	80
Memorial Sloan-Kettering (56)	5-Fu: 750 mg/m^2/5 days* Mito: 15 mg/m^2 d 1	30 Gy/15 fx	42	23	0	82
RTOG (57)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10 mg/m^2 d 2	40.8 Gy/24fx	79	8	0	73 (3y)
Highland Hospital (58)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10 mg/m^2 d 2	50-57.5 Gy/ 25-32 fx	33	4	0	
Fresno Community Hospital (59,60)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10-15 mg/m^2 x2	41-50 Gy/ 23-28 fx	30	1	0	90
Norwegain Radium Hospital (61)	5-FU: 1000 mg/m^2/4 days* Mito: 10-15 mg/m^2	50 Gy/25 fx	94	17	3 (3%)	72
Istituto Nazionale Tumori, Milano (62)	5-FU: 750 mg/m^2/5 days 2–3 cycles* Mito: 15 mg/m^2	54 Gy/30fx (split)	38	6	0	
Princess Margaret (63,64)	5-FU: 1000 mg/m^2/4 days* Mito: 10 mg/m^2 d 1	48–50 Gy/ 24-20 fx (split or continuous)	69	10	0	65
	5-FU: 1000 mg/m^2/4 days*	48-50 Gy/ 24-20 fx (split)	66	18	1 (2%)	64
M. D. Anderson (65)	5-FU: 300 mg/m^2/days for 32 days (median)*	45 Gy/25 fx	25	8	1 (4%)	
Ochsner Clinic (7)	5-FU: 1000 mg/m^2/5 days and days 31-35 Mito: 10 mg/m^2 d1	40 Gy/20 fx	35	9	0	87

5-FU, 5-fluorouracil; Mito, mitomycin C; fx, fractions.
*Continuous 24-hour infusion.

Poorer local control was reported by the M. D. Anderson Cancer Center group when low-dose 5-FU (300mg/m^2/day) was used throughout the irradiation course (45-66 Gy). (54) Local control without an abdominoperineal resection was 67% in 24 patients, but 9 of 10 patients who received at least 55 Gy were controlled. Toxicity was considerable, with 6 of 25 patients experiencing grade 4 diarhhea, resulting in the death of 1 patient.
Radiation Therapy Oncology Group study is currently underway comparing irradiation (45Gy) and concurrent 5-FU to irradiation plus concurrent mitomycin and 5-FU. This trial, which is nearing its projected accrual, addresses the role of mitomycin. Patients with positive biopsies after initial treatment are eligible for cisplatin-based chemotherapy treatment, which addresses the issue of additional chemotherapy in poor-risk patients. Because the definitive results of this trial are not yet available, it is too early to conclude that mitomycin is not a necessary part of therapy, especially because the complications related to the use of this agent are quite small.
The chemotherapy regimen of mitomycin and 5-FU is quite active against anal canal tumors, but some patients do not respond or have less than a complete remission with this combination. The effectiveness of cisplatin-based treatment for patients with advanced disease has made use of this agent as part of multimodality therapy attractive. A few trials investigated the use of cisplatin with 5-FU anf irradiation for initial therapy with promising results, especially for high-risk patients. (75-79)

Radical surgery. Before the widespread use of multímodality therapy, more than 90% of patients with potentially curable anal canal cancers required abdominoperineal resection. A wide perineal dissection in association with a posterior vaginectomy in women was recommended. (28,80) Despite initial enthusiasm of the oncology group at Memorial Sloan-Kettering Cancer Center for vaginectomy, á more recent analysis discounted its routine application. (14) Lateral pelvic lymphadenopathy was initially advocated by the same group on the basis of a 24% incidence of pathologically positive nodes. (27) Subsequent analysis could not define any therapeutic benefit for this extended abdominoperieal resection. (14) The overall cure rate with abdominoperineal resection is approximately 50%. (81) Some reports show that wide resections of the canal carcinomas with continence preserving could be feasible and curative. (82)
The Mayo Clinic experience initially reported in 1976 by Beahrs and Wilson (33) was updated by Boman and associates. (51) Disease recurred in 40% of the 114 patients, with subsequent treatment resulting in a 71 % 5-years survival rate. The M. D. Anderson Hospital group reported a 62% 5-year survival rate for 109 patients treated with only abdominoperineal resection. (39) One sixth of the cases were anal margin cancers. A Memorial Sloan-Kettering Cancer Center update included 103 patients treated by radical surgery, with a 55% 5-year survival rate. (53) All of these tumors involved the dentate line. The 5-year survival rate for patients with tumors larger than 5 cm was only 40%. At St. Mark's Hospital, the 5-year survival rate among 83 patients with anal cancers involving the dentate line treated by radical surgery was 48%. (12)
Treatment failure despite radical surgery is locoregional and distant. In the Mayo Clinic experience, 84% of initial sites of failure included local and regional disease. (51) Most cancer-related deaths are secondary to uncontrolled locoregional tumor. One third to one half of patients with locally advanced anal cancers treated by abdominoperineal resection at the major centers known for their expertise in this disease still had local recurrence in the pelvis or perineum. (12,28,39,51,53)
With the success of combined modality therapy, abdominoperineal resection should be reserved for salvage of the few patients in whom multímodality treatment fails or for morbidity related to therapy, such as severe proctitis.

Table 1. Results of Multimodality Therapy for Anal Canal Carcinoma

Investigations	Chemotherapy Regimen	Radiation Therapy Regimen	Patients Evaluable	Abdominoperineal Resection Performed	Treatment Related Deaths	5-Years Survival (%)
Wayne State (55)	5-Fu: 1000 mg/m^2/4 days 2 cycles* Mito: 15 mg/m^2 d 1	30 Gy/15 fx	104	31	0	80
Memorial Sloan-Kettering (56)	5-Fu: 750 mg/m^2/5 days* Mito: 15 mg/m^2 d 1	30 Gy/15 fx	42	23	0	82
RTOG (57)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10 mg/m^2 d 2	40.8 Gy/24fx	79	8	0	73 (3y)
Highland Hospital (58)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10 mg/m^2 d 2	50-57.5 Gy/ 25-32 fx	33	4	0	
Fresno Community Hospital (59,60)	5-FU: 1000 mg/m^2/4 days 2 cycles* Mito: 10-15 mg/m^2 x2	41-50 Gy/ 23-28 fx	30	1	0	90
Norwegain Radium Hospital (61)	5-FU: 1000 mg/m^2/4 days* Mito: 10-15 mg/m^2	50 Gy/25 fx	94	17	3 (3%)	72
Istituto Nazionale Tumori, Milano (62)	5-FU: 750 mg/m^2/5 days 2–3 cycles* Mito: 15 mg/m^2	54 Gy/30fx (split)	38	6	0	
Princess Margaret (63,64)	5-FU: 1000 mg/m^2/4 days* Mito: 10 mg/m^2 d 1	48–50 Gy/ 24-20 fx (split or continuous)	69	10	0	65
	5-FU: 1000 mg/m^2/4 days*	48-50 Gy/ 24-20 fx (split)	66	18	1 (2%)	64
M. D. Anderson (65)	5-FU: 300 mg/m^2/days for 32 days (median)*	45 Gy/25 fx	25	8	1 (4%)	
Ochsner Clinic (7)	5-FU: 1000 mg/m^2/5 days and days 31-35 Mito: 10 mg/m^2 d1	40 Gy/20 fx	35	9	0	87

5-FU, 5-fluorouracil; Mito, mitomycin C; fx, fractions.
*Continuous 24-hour infusion.

Poorer local control was reported by the M. D. Anderson Cancer Center group when low-dose 5-FU (300mg/m^2/day) was used throughout the irradiation course (45-66 Gy). (54) Local control without an abdominoperineal resection was 67% in 24 patients, but 9 of 10 patients who received at least 55 Gy were controlled. Toxicity was considerable, with 6 of 25 patients experiencing grade 4 diarhhea, resulting in the death of 1 patient.
Radiation Therapy Oncology Group study is currently underway comparing irradiation (45Gy) and concurrent 5-FU to irradiation plus concurrent mitomycin and 5-FU. This trial, which is nearing its projected accrual, addresses the role of mitomycin. Patients with positive biopsies after initial treatment are eligible for cisplatin-based chemotherapy treatment, which addresses the issue of additional chemotherapy in poor-risk patients. Because the definitive results of this trial are not yet available, it is too early to conclude that mitomycin is not a necessary part of therapy, especially because the complications related to the use of this agent are quite small.
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Locally Advanced, Residual, or Recurrent Cancer

Anal Margin Cancer

Recurrent anal margin cancer, after local excision, may require further local excision for salvage. In a study from Memorial Sloan-Kettering Cancer Center, 16 patients in whom disease recurred underwent additional surgical procedures; of these, 12 were alive at 5 years, and only 2 had died of disease. (83) One patient was unavailable for follow-up. Eleven of the 12 patients with local failure underwent local excision only for salvage. More advanced primary or recurrent anal margin lesions may be salvaged by external radiation therapy. (84)

Residual Anal Canal Cancer

Whether anal canal patients are treated by radiation therapy alone or chemoradiation therapy, histologic confirmation of complete remission should be obtained several weeks after irradiation is completed.56 Patients with clinically complete remissions but microscopically residual superficial tumors should undergo sphincter-sparing wide local excisions. The deep margin may be increased by including a portion of the internal sphincter, with minimal impact on subsequent continence. If the margins are positive, an additional radiation boost may be used, if feasible, with external beam or an interstitial implant. If a radiation boost is not possible because maximal radiation has already been delivered, an abdominoperineal resection is probably required for cure, what yields up to 72% 3 year survival rate. (85)

Recurrent Anal Canal Cancer

Patients with recurrent anal canal cancer after surgery should be considered for multimodality therapy. Locoregional failures after initial multimodality therapy have been successfully treated with abdominoperineal resection (2,85) or with additional irradiation and chemotherapy. (59) The success rate of surgical salvage averaged about 60% for seven series (54,57,63,86-89) ,but only 29% in some others (85). Mitomycin plus 5-FXJ can also induce major remissions in previously treated patients who have locally recurrent disease. (90)

Locally Advanced Anal Canal Cancer

Multimodality therapy for locally advanced primary anal canal tumors may yield good palliation and, in some cases, cure. In a study reported from the University of Virginia, major regressions of disease were observed in 6 of 7 patients, 3 of whom were treated with chemotherapy alone and 3 with chemotherapy plus irradiation. (91) Abdominoperineal resections were performed on all patients, and all had delayed wound healing. Three of the 7 patients remained disease free for 24 to 26 months and 4 died, 2 of cancer and 2 of other causes. Another form of multimodality therapy mitomycin and 5-FU with external and interstitial irradiation. (92) Ir implant, was tried in 29 patients with advanced local disease. (93) After a follow-up of 5 to 54 months, 25 of 29 patients were alive and free of disease; only 2 patients required radical salvage surgery with loss of sphincter function. Papillon achieved a 90% local control rate in T3 tumors larger than 4 cm in diameter with a combination of mitomycin, 5-FU, external irradiation, and an 54 Ir implant. (94)

Brachytherapy combined with external irradiation has been used for advanced disease. (94-96) There was a 70% local control rate in Papillon's analysis of T3 tumors larger than 4 cm in diameter, which were treated with (97) Co external irradiation and an (92) Ir implant without combined chemotherapy.

Inguinal Node Involvement

The initial experience suggested that patients with grossly positive inguinal lymph nodes synchronous with the primary tumor were incurable. (98) A subsequent report indicated that 2 of 13 patients survived 5 years after abdominoperineal resection, followed 6 weeks later by inguinal lymphadenectomy. (99) Other studies confirmed a small cure rate for surgical treatment of patients with synchronous unilateral inguinal nodes. (10,33) External irradiation (84) postoperatively may improve these results slightly, but radical external irradiation alone (84,86,88,100) can achieve a nodal control rate of about 65%, and external irradiation combined with chemotherapy (58,101,102) can achieve nodal control in approximately 90% of patients. Current recommendations are for limited surgical sampling, combined chemotherapy and radiation therapy with boost doses to the involved groin (45-50Gy); surgical salvage may be done for isolated inguinal recurrence.

The development of unilateral metachronous inguinal lymph nodes usually does not carry such an ominous prognosis. After therapeutic groin dissection, the 5 to 7 years survival rate reported from Memorial Sloan-Kettering Cancer Center and St. Mark's Hospital exceeded 50%, (29,83) but it was zero in a small series reported from the other hospitals. (33) Current strategies in patients with metachronous isolated inguinal node metastases after multimodality therapy include a formal groin dissection followed by chemotherapy. The use of radiation under these circumstances depends on prior dose and fields.

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MULTIMODALITY TREATMENT OF ANAL CANCER. EXPERIENCES IN 142 PATIENTS

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Introduction: Since the early 80th therapy of anal cancer changed considerably with the introduction of multimodality treatment by Nigro. Untill than monotherapy, mainly by surgery, was predominant, leading to anorectal excision in the anal canal cancer, in restricted cases of the anal margin to local excision. Although anal cancer should be early diagnosed, the majority presents in an advanced stage, at least one third with a loco-regional or distant metastasis. Accounting this and in order to preserve continence these superficially lying tumors with moderate susceptibility to irradiation unterwent radiotherapy too. However, the results of both, reaching about 50% 5 years survival, were equal, but not satisfying at all. The combination of both may improve to about 70 %, but regulary resulted in loss of continence.

THE MULTIMODALITY TREATMENT.

The Nigro-procedure.

The concept of Nigro was to increase the effect of radiotherapy by additional chemotherapy (5-FU + mitomycine - C), so that even lowering the dosage of radiotherapy to 30 Gy was possible, and to apply radical surgery 6 to 8 weeks later. By this cure rates could be improved to more than 80 %, a lot of surgical specimens showing no residual tumor. These observations made it possible to restrict indication for anorectal excision to cases of persisting tumors and larger ulcerations, especially if they presented with sphincter defects, meaning round about 20 - 30 % of all cases, thus preserving continence function in the others by local excision of the prior bed of the tumor. Fascinating in this concept has been the very moderate irradiation dose of 30 Gy, because the former dosage of 60 Cry may lead to considerable deterioration of sphincter function expecially in elder patients.

Own results in the first period.

In 1981 1 adapted this concept for potentially curable tumors (<Tx Nl MO). Regarding the former experiences the results were amasingly good. In merely 80 % there were no macroscopical signs of residual tumor after the initial treatment.In each 10 % as well patients presented with persisting gross tumors or ulcers, impossible to decide, whether they had remaining cancer. Only these underwent radical ano-rectal-excision, whereas the others were revided locally. Histologically 2/3 of the ulcers showed no residual tumor; in case of local excision 15 % had microscopical tumors, but these cells presented with marked irradiation damage. Consequently only three of these patients developed local recurrence. In summary on a histological basis the initial therapy failed in 20 of 78 patients, however one may discuss, whether those tumors, which had been macroscopically cleared, have been failures at all from a biological point of view because only 3 of 9 developed recurrence after local excision. Cancer related mortality rate was 6 patients of 66, surviving 5 years, the survival rate therefore 90 %.

Further developments since 1990

Seeing an initial rate of failure of about 30 % it seemed possible to reduce this quote by increasing radiotherapy to a dosis of 50 to 60 Gy. This we did in 1990. Since than 64 patients underwent this modification. Regarding the foregoing experiences the surgical procedure was altered too. Local excision was even done in primary advanced tumors (T3 and T4), now including residual ulcers too, if they did not exceed 2 cm. If the tumor ha s been large in diameter, but was cleared by chemo-radiotherapy, local revision took place by multiple biopsies. If there has been residual gross tumor at the anal margin, it was managed by local excision too. Thus the indication to anorectal excision could drastically be reduced to totally 4 cases, 2 primary and 2 on account of local recurrence. The initial rate of failures droped to 11 % (9 of 64), that enabled to preserve continence in 94 % of the patients. This, however, is the most remarcable result, because the late results - very good akeady -could not be improved furthermore (5 local recurrences, 5 cancer-related deaths).

On the other hand the higher radiation dose led to an increase of therapeutical side-effects. Whereas in the former series merely none had local effects of radiotherapy, I now observed 28 cases with persisting moderate or even severe (6) dermatitis and/or proctitis, furthermore 9 patients with deterioration of continence, 6 degree I, 3 II. However none of these would accept a stoma on account of the incontinence.

Some last remarks to therapeutical outcome: We had totally 3 deaths according to treatment, 2 by chemotherapy (cardiac failures), 1 by anorectal excision.

Overall failure of total primary therapy was 12 of 142 (8,4 %).

Conclusions

Multimodality treatment is very effective in locally restricted anal cancer with a survival rate of about 90 %. In increasing the irradication dose to 50 - 60 Gy local tumor control will be gained in 90 %, enabling preservation of continence in 94 %, because surgery can be restricted to local excision or revision in the vaste majority of the cases.

On the other hand there remain at least three questions open for discussion:

1. What would be the most convinient dosage ofradiotherapy, because the actual dose is rich in side-effects, and
2. may there be other regimens for chemotherapy, because mitomycine is problematic?
3. Does chemotherapy only work as a radiosensitizer or is there still an additional local and systemic effect, because the number of distant metastases is considerably low. But if so,would be worthewhile to continue chemotherapy in cases, which had residual tumor in the surgical specimen?

SURGICAL DECISIONS IN ANAL RECTAL CROHN'S DISEASE

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Introduction: Anorectal lesions are most frequent in Crohn's disease.However valid epidermiological data are not available. It is estimated that overall round about 40% of all diseased people will suffer from anorectal manifestations. The possibility, to develop anorectal symptoms, depends on the site of the main intestinal infection. It increases from 20 %, if only the small intestine is involved, to 40 % in ileocolic disease, more than 60 % in distal colonic manifestation and almost 100 % in rectal illness. Moreover in 10 to 15 % anal manifestation is the first sign of disease, proceeding the intestinal outbreak from months or even several years. The severity of anorectal lesions, too, is related to the site of the intestinal location, the more distal the more complex they are.

Morphological appearance

The far most dominant lesions are fistulas and abscesses. The morphology of fistula is wide spread from superficial clinically mostly inapparent subcutaneous forms to very complex fistulous systems extending to the gluteal, inguinal, femoral or even abdominal region. The more complex they are, the more often they will form painfull abscesses and expand via spontaneous or surgical drainage by new fistulous tracks. However although these forms seem chaotic, there are still certain rules, which will leed to adequate surgical intervention:

- Even in Crohn's disease the majority of infections follows a crypto-glandular pathway, as known from ordinary anal fistula, especially if the distal colorectum is free of disease. These I call fistula with Crohn's disease, whereas the following ones may be called Crohn's fistula,especially as most of them histologically offer the characteristical signs of Crohn's inflammation: epitheloid granulomas.
- The peripheral spread is almost superficial, imitating a fistulous pyodermia.
- Even very complex systems originate frome one, seldom two or three central abscesses, located in the immediate neighbourhood of the primary ano-rectal Crohn-lesion.
- Most of these abscesses are located in the ischiorectal fossa, the primary lesion situated at or a little bit of the dentate line, not seldom associated with a circumscript anorectal stenosis.
- If in women central abscess developes perineally, its depth induces drainage pathways to the vulva misleeding to the diagnosis of Bartholinitis, or more often to vaginal fistulas. These forms are regulary accompanied by mild to severe anorectal stenosis.
- Pelvic abscess is more often induced by ascension of incompetent drained ischiorectal abscess than primary pelvic origin. If there is primary pelvic infection it mainly results from severe rectal manifestations, but occasionally from fistulous ileitis or - more seldom - from sigmoiditis.

Besides fistulas and the already mentioned very typical stenosis we observe ulcers - the term "fissure" should be avoided, because it may induce false therapeutical decisions - the border of these ulcers often undermined with a tendency to putride retention and thereby forming shorttracked superficial fistulas, furthermore tags, sometimes eaching very giant forms, and various manifestations of dermatitis. Occasionally cancer will originate within fistulas - none of the cases, I've seen untill now, was diagnosed clinically! Cancer can develope very shortly, in one case within duration of fistula shorter than one year in a 22 years old woman, so that it may be possible, that cancer may be the first and fistula developed on the condition of cancer.

There seem to be constitutional signs for developing anal lesions, because these patients have a very short anal canal, the anoderma not exceeding 1 cm, and a reduced internal sphincter. The integument appears very soft, almost frail, lividly discoloured.

Local surgical procedures

Predominant aims of surgical interventions are:

- local control of infection and - even by this-
- preservation of continence function.

Local control primarily does not intend to eliminate the fistula at all means. What is causing complaints, is the insufficient drainage of periano-rectal infection. However, all inflamed perianorectal tissue can be removed surgically. What is to be done with the transmural part of the fistula is a second question, the answer of which concerned into the relation to the anal sphincters. If it passes below the midle of the anal canal, you can lay it open too and more than 90 % of these fistula will heal completely. If it is above, you will place a seton drainage. Thereby you will have complete control of infection. What should be done with the remaining part of the fistula, is the third question.

This procedure demonstrates two severe differences to ordinary fistula-surgery:

1) It is not as radical, as you have to respect a greater part of the sphincter, because as Crohn's patients are always in danger to suffer from diarrhoe, it is necessary, that the remaining sphincter portion is able to control.

2) Local control of infection is unavoidable to prevent secondary sphincter damage by the infection itself. In this context Alexander-Williams is often cited, that incontinence in Crohn's disease is not due to aggressive disease, but aggressive surgeons. This may result, if you neglect my first conclusion, but it is incorrect in its first appointment. Crohn's disease is a destructive disease, and meanwhile I know a lot of patients, who have incontinence because of insufficient local control, and the more others, who preserved continence on account of adequate surgery.

On the other hand, this shows the ongoing dilemma in Crohn's disease, because you are unable to cure it. This leads to the answer of the third question. As it is so, you never will be sucessful with fistuloplasty. Even if you have complete remission unter the protection of a stoma and the fistula cured under these circumstances, it will relapse soon after removal of the stoma. Therefore I never arrange a stoma only on account of a fistula.To my opinion there are only two indications to establish a stoma in ano-rectal Crohn's disease:

- severe rectal manifestations in patients, who desire to take even the most inferior chance to preserve the natural pathways, but I know only very few, where it has been sucessful and than mostly for a shorter period.
- Patients, who already have sphincter damage and will need difficult reconstruction procedures to regain continence function, and this under the condition, that the rectum is free of disease and the anorectal lesions are completely healed.

If I do a fistuloplasty despite of these considerations, I do in cases, who have severe complaints of false-ways-production expecially in large recto-vaginals fistulas, and I do primary in the hope, not to heal the fistula, even if it may happen for some times and for a while, but to reduce the diameter of the fistula, so that false-way production would not be a greater problem further-more.

So as you cannot heal Crohn's disease, in other words, if you can't beat it, than peace it. That is, to transforme the lesion from a painful one to one of no or even minor complaints. This means to accept a residual fistula, which has become so scar-

red or - better - has got an epithelial overleaf, so that is unable to expand again. Using the method of excisional drainage, You have to calculate duration of the seton-drainage for at least 1/2 to 1 year. Such a remaining fistula will than almost be a cosmetical rather than a pathological defect.

Decisions in intestinal and anal disease

The main question is, what is prior to the behaviorship of the patient. Relationship of one to another is only loose: removing the intestinal lesion will not automatically improve the anorectal. On the other hand, if in a wide-spread ano-rectal manifestation you get control over the infection, the patients may considerably recover in general. Nethertheless the intestinal lesion is superior to the anal. Than you have to decide, wether it could be managed conservatively or has to been operated on.

- If there is a concervative option, than you should manage the fistula as described above.
- If surgery is unavoidable for the intestinal manifestation, an inactive fistula may be left behind, but if it is prutride, you should use the time of preparation for the operation to do excisional drainage. Preparation means functional exclusion of the bowel by parenteral nutrition for at least 2, better 4 weaks (or even longer, if necessary).

The next question is that of extension of intestinal disease.

- If you have ileitis alone, than there are merely no problems.
- If you have colitis, but the rectum is free, than resect the colon, but leave the rectum behind blindly closed and establish a terminal ileostomy according a Hartmann's procedure. This total exclusion of the anorectum will give a good chance to overcome with the anal lesions. Having control over the periano-rectal infection the presence of a residual sufficiently drained fistula does not hinder restoration of fecal passage. To have sufficient function in number and quality of stools as continence as well, You will need round about 15 cm of a disease-free rectum.
- If the rectum is affected too, than you have really no chance to preserve continence. Than you shall do a subtotal proctocolectomy, cutting down the rectum to the level of the fistulas, but leave anus and distal rectal stump behind, once to diminish the surgical trauma, but mainly to prevent expansion of the fistulous infection to the abdominaly cavity. But tend to leave only a very little rest of rectum, which may be exstirped perineally later on without reentering the abdomen.
- Whether the remaining stump has to be removed later-on, depends on development of disease in this region. If it becomes inactive by exclusion, you can wait and see. You have to regard that in case of necessity of rectal excision these wounds have to be left open and very often show great disadvantages in healing, sometimes persisting for several years. So rectal excision should be restricted to cases with ongoing severe complaints.

Conclusion

Dealing with anorectal manifestation of Crohn's disease needs great experience. Although there are certain rules in development of disease and its stage-adjusted therapy, cases are very individual and extension of disease often exhibits during operation at first. Furthermore the concomitant intestinal manifestation has to be taken into therapeutical considerations, resulting in a complex schedule of decisions. Finally you are confronted with a disease, which is uncurable untill today. So concerning anorectal lesions we learned again, what we already knew from intestinal lesion, that minimal surgery is superior to aggresive, this means in an final conclusion: the surgical task is to eliminate those alterations, which are due to complaints, but may leave behind residual disease, a patient will overcome with.

TOTAL MESORECTAL EXCISION - ITS ROLE IN RECTAL CANCER SURGERY

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The concept of total mesorectal excision (TME) has grown over twenty years from a surgical hypothesis into a major international training initiative. Throughout this period scepticism and sometimes outright antagonism have slowed progress and threatened to strangle the idea that surgical detail might be more important than the combined multidisciplinary might of the adjuvant modalities. As always, the arguments for surgical precision are easy to dismiss because of the absence of prospective randomised trials. As Silen pointed out in a letter to the Lancet (1). The likelihood that a proper randomised trial will ever be carried out to test whether total mesorectal excision (TME) provides an advantage over conventional operation is remote. He went on to express the opinion that. Is it then appropriate to dismiss the comparison with retrospective controls and eschew the use of a procedure which seems so superior in terms of both local recurrence and survival? In my view it is unconscinable to do so (1).

It is sad to reflect that statistical scientific brains in many countries continue to dismiss the lack of controlled trials as indicating that the claims for T M E can be safely ignored Wolmark, evidently contemplating the dubious fruits of various N S A B P trials with great satisfaction, expresses his current view that „in the light of these results it is difficult to rationalise surgical techniques such as mesorectal resection". The Basingstoke response is a lifetable from a twenty year follow up programme of 480consecutive rectal cancer operations with no significant contribution from adjuvant therapies. Concentration on T M E has delivered a 78% 5 year cure rate in those without obvious metastases at the time of presentation with ±4% at 95% confidence intervals. At ten years the figures became 73% ±8%. These date make it possible to state that rectal cancer is a locoregional disease in three quarters of those who have not already spread to the liver or elsewhere. Such patients after surgery should honestly be told that there is a three to one chance that they do not need chemotherapy, and a three to one chance that it will not work if they are the unlucky one who needs it.

In discussing advances in surgical technique in this way other workers ignore the realities of surgical practice and the fact that no improvement in the detail of surgical technique has over come about as a consequence of a prospective randomised trial. None of the established operative procedures in daily practice has been established in this way. It is not difficult for a practical surgeon to comprehend why the prospective randomised trial a „non starter" in this setting. If randomisation is between different surgeons the superiority of one over the other may reflect any of a hundred differences in their technique. If the T M E surgeon, taking 3-4 hours to produce a perfect T M E specimen, is asked to switch in a half of his patients to a rapid „wrenchout" of yesteryear he simply refuses to do so. One can randomise drugs or adjuvants, or even surgical methods such as incisions or the use

of the laparoscope - in rectal cancer one cannot randomise what is so important - the surgeon's worths moment, his worths cut or tear into malignant tissue.

Thus the progress of T M E in particular has been substantially slowed by insistence on randomised trials as the gold standard for progress. Indeed it is crucial that the very evidence which rated highest on the quality of evidence scale in the recent guidelines issued by the Association of Coloproctology and The Royal College of Surgeons have in fact led to progress in what most doctors most closely concerned with the actual patients would consider a harmful direction - the more widespread use of chemotherapy, particularly as an adjuvant modality, and the use of radiotherapy in the post-operative setting. When applied thus to the new pelvic contents after reconstructive sphincter preserving operations it leads to debilitating side effects and has a very cruel impact on the patient's quality of life. Despite this it is widespread use throughout the U. S. and Germany, although real evidence of oncological benefit is largely lacking.

We thus have two major international trends which owe their reality to our obeisance to what one Japanese Professor has called the „English randomising disease". The care of rectal cancer patients is indeed a multidisciplinary process, but each discipline's skills and concentrations depend entirely upon the policy which is decided upon in relation to the surgery. In Norway, Sweden, Denmark and Holland formal national T M E projects are underway, whilst in Germany, Austria, the U K, and several other countries major initiatives are being undertaken to implement training in the detail of the technique of the surgery. The role of the other key disciplines in each of these countries is thus bound to be completely different. In Norway neither radio nor chemotherapy is in regular usage except as a component of the Nordic trials. In Sweden pre-operative short course radiotherapy 5x5 Gy in 5 days as an immediate pre-operative modality is almost standard for all except T 1.2 tumours. In Holland the major trial of supervised and standardised T M E surgery with randomisation of short course pre-operative D X T will certainly become a classic milestone.

In most countries the idea has gradually become accepted that the fixed advanced and perhaps even locally „inoperable" tumour should receive long course radiotherapy of 50-55 Gy over six weeks followed by a period of another 4-8 weeks for anatomical regression to occur and for hyperaemia to settle. During this time a desmoplastic reaction and a sclerosing process around the margin of the T M E specimen make the „holy plane" less areolar and a little more difficult - but not usually impossible. In many cases the surgeons may well surmose that the original advanced tumour would have made dissection more difficult or the production of an uninvolved T M E margin impossible, or even that pre-sacral venous bleeding may have been prevented by D X T occlusion of the veins. We are left then with the reality that we must manage patients with methods and protocols that are based upon inadequate evidence. If T M E is indeed becoming as MacFarlane recently predicted, the new „Gold Standard" the the surgeon's job is technically difficult but intellectually easy. If Quikels circumferential margin involvement (C M I) examination becomes the immediate audit tool then the key role of the histopathologist will become similiarly established. Reports from individuals and groups will begin to include, as is becoming standard in Holland, the percentage of C M I positives as a quality measurement.

In the future the refinement of M R I with various enhancement modalities will combine with C M I histology and „Holy Plane" surgery to focus attention on the interface between mesorectum and surrounding tissues during the planning stage. The key role of the radiologist will be to predict the threatened or involved margin. M R I will become the key investigation for the fixed or tethered tumour. Nodal involvement will remain an important component of pre-operative staging, but more to define the relationship of nodes to margins than to count their numbers. Total mesorectal excision is the appropriate block dissection for rectal cancer and there is no evidence that the existence of involved nodes constitutes an indication for radiotherapy before surgery. In rectal cancer, in contradiction to colon cancer, there seems little evidence that nodes constitute an indication for chemotherapy afterwards either, though its use in this situation is widespread. Endorectal ultrasound will probably lose ground to M R I because of its relative inability to define the mesorectal margin, though it may remain useful in the region of the sphincters for identifying T1 tumours for local excision. Where expertise has been built up it will remain useful but the dream of an „off the shelf M R I analysis of all the details of the tumour must surely be achievable within the next decade. It's key advantage will be that M R I prediction of an involved or dangerous margin will ultimately become the selection factor for preoperative irradiation, since radiotherapy has the key advantage of „sterilising" the margins which Quirke has shown to be key focal points of surgical failure. As Pahlman points out „radiotherapy fails centrally, surgery fails at margins". The science of radiation oncology is developing so as to dictate better co-operation between the disciplines in other important ways too. For far too long pre-operative radiotherapy has been ordered without the radiotherapist even being told whether the surgeon plans to preserve the anal canal or remove it. In their classic paper from the Karolinska Holm et al pointed out the desirability of anal sparing which has hitherto not been a part of the routine even in that distinguished institute. It must surely become standard practice for both the surgeon's plan and the full M R I analysis of marginal tumour proximity to be the key components of the wotkup for radiotherapy planning in future. With the great advances in anaesthesia and the widespread use of epidurals operative martalities have fallen despite surgery on older and sicker patients. The single biggest killer however, stands out even more glaringly as improvements in other areas become apparent - anastomotic leakage. The advent of the colon pouch has reduced the leakage rate in the Basingstoke series from 11% (clinical) plus 6% (radiological only) to 2,5% plus 2,5%, but almost all of these have been defunctioned. The Basingstoke Unit is currently running a randomised trial between conventional defunctioning by proximal stoma and a new soft silicone anal stent. It is my personal view that leakage in the-ultra low anastomosis is quite simply explained by the tightly closed anal sphincter, made more dangerous by the absence of the rectoanal inhibitory reflex after surgery. If the stent solves the problem by making positive intra rectal pressures impossible then the reluctance of so many surgeons to defunction will perhaps cease to cost a small but persisting trickle of unnecessary deaths.

Summary: Surgeons face a special challenge in implementing the long demanding precision of a good T M E. Histopathologists are already rising to the unique opportunity of becoming the principal auditor of these surgical skills. If T M E is accepted as the relevant block dissection for rectal cancer and the key importance of margins in selection for radiotherapy becomes established then the way forward for the radiation oncologists and the radiologists becomes clear. The place of chemotherapy in rectal cancer has yet to become clear, but its use as a neo-adjuvant pre-operative modality offers the most exciting prospects, and may well eclipse the rather small achievements of its use hitherto in the post-operative setting. The authoris personal view is that the ability of all the disciplines to influence survival in rectal cancer has been largely exercised by the time the surgeon retires to bed on the nigh after the operation.

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ENDOANAL SONOGRAPHY IN PERINEAL SEPSIS

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Introduction: In the past decade there has been a resurgence of interest in the use of endoluminal ultrasonography for a variety of anorectal applications.
The introduction of technology that allows real-time 360° radial scanning of the anorectum and the surrounding structures began a new era in endoluminal imaging. The ability of accurately stage rectal cancer preoperatively was the first real benefit realised by the use of this new modality; many other useful applications in the field of colorectal surgery have since become apparent.

Generality

Ultrasonography is an imaging technique whose principle is based on the interaction between transmitted sound waves and the juxtaposed different tissue densities of the body. A transducer emits pulsed sound waves of a specific frequency with defined depth of penetration through the tissue layers. The sound waves pass through tissue planes, and at each interface between different tissue densities and acoustic impedance, some of the sound waves are reflected toward the transducer. The time difference between sound transmission and reception is calculated, and an image is generated by the digital sequential processing of a multitude of sound waves (5). The rectum and anal canal are well suited for ultrasonographic evaluation because of the variety of tissue density interfaces present in this readily accessible region.
Ultrasonography is less expensive, relatively quick and is well tolerated by the patient. Moreover, the patient is not exposed to radiation during the course of the examination.
The examination can also be performed as an intraoperative procedure, which may be helpful for detecting abscess cavities, fistula tracts, or internal openings.
Endoluminal ultrasonography has emerged as one of the newer diagnostic examinations that can complement the clinical examination and therefore provide relevant information with a direct impact on planned treatment.

Technique of Endoanal Ultrasonography

There is no need for sedation, and therefore no need for specialised monitoring. The patient is placed in the gynecologic position. A digital rectal examination serves the dual purpose of excluding significant anal stenosis and lubricating the anal canal.
We currently use the 1846 Brüel & Kjaer (Naerum, Denmark) scanner and a 7.0 M H z 8539 transducer with a focal length of 2 to 5 cm. A small finger cot balloon is placed over the transducer and properly secured in place.
It is not necessary to use expensive degassed saline water as long as all bubbles have been evacuated from the water. By convention, the ultrasound probe is held with the spigot in the upright position, and the probe is maintained in the centre of the lumen. A sonolucent, tapered plastic cap is placed over the transducer. This cap is then filled with water and all bubbles are removed.
A condom containing ultrasound gel is placed over the probe, and this is lubricated with a water soluble lubricant.

Endoanal Ultrasonography

Normal image

Tjadra et al. (11) have performed elegant post-mortem and clinical studies and have identified the anatomic layers that correspond to the anal ultrasound images. The mucosa-submucosa complex typically appears as a hyperechoic band adjacent to the transducer and the cap. The internal anal sphincter is observed as a hypoechoic circle.
The internal anal sphincter has an average thickness of 2 to 4 mm which seems to increase with advancing age (1). There is no correlation between me sonographically determined anal sphincter thickness and the mean maximum resting pressure (4).
The external anal sphincter is a striated muscle that appears sonographically as a mixed echogenic band outside the hypoechoic internal anal sphincter. The outside borders of the external anal sphincter with the perirectal fat are not clearly defined (9).
It is easy to divide the anal canal into upper, middle and lower thirds based on anatomic lendmarks. At the level of the upper anal canal, the puborectalis muscle sling is observed as mixed echogenic U-shaped band, which encircles the rectum posteriorly (Fig 1).
Because of the sling anatomy of the puborectalis muscle, there is a hypoechoic gap anteriorly, which can be easily confused with anterior sphincteric defect. By filling a latex balloon with water or by introducing the finger in the vagina it is possible to avoid this artefact and measure the thickness of the anterior wall (Fig 1).
The hypoechoic internal anal sphincter becomes more prominent, and the anterior quadrant is replaced with the circumferential mixed echogenic fibers of the external anal sphincter. The middle canal is defined as the level of maximum wide internal anal sphincter (Fig 2). At this level the majority of sphincteric defects are discovered.
At the lower anal canal level, the majority of the musculature is the mixed echogenic subcutaneous portion of the external anal sphincter (Fig 3). This level of the anal canal may be the site where internal openings of anal fistulas are discovered.

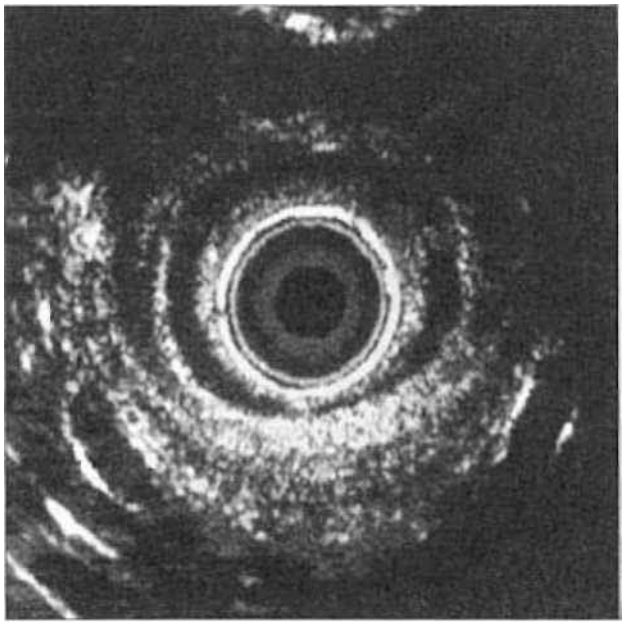

Fig.1
Endoanal ultrasound at the level of the upper anal canal.
Puborectalis muscle sling course posteriorly around the rectum.
The relative lack of muscle fibres anteriorily is normal anatomy.
By introducing the finger in the vagina it is possible to avoid this artefact and measure the thickness of the anterior wall.

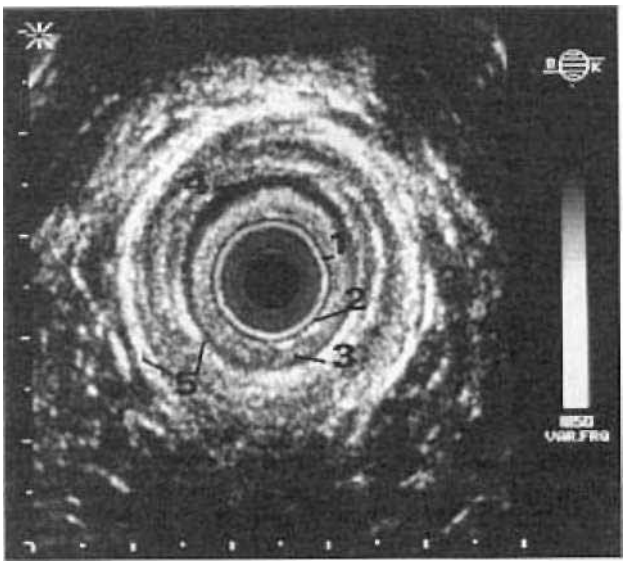

Fig. 2
Normal endo-anal ultrasonography of the medial part of anal canal.
1. hyper-echogeneous layer: space between the balloon and the mucosa
2. hypo-echogeneous layer: mucosa
3. hyper-echogeneous layer: submucosa
4. hypo-echogeneous layer: internal sphincter
5. hyper-echogeneous layer: (internal arrow) longitudinal muscle mixed echogeneous layer (between the two arrows): external sphincter

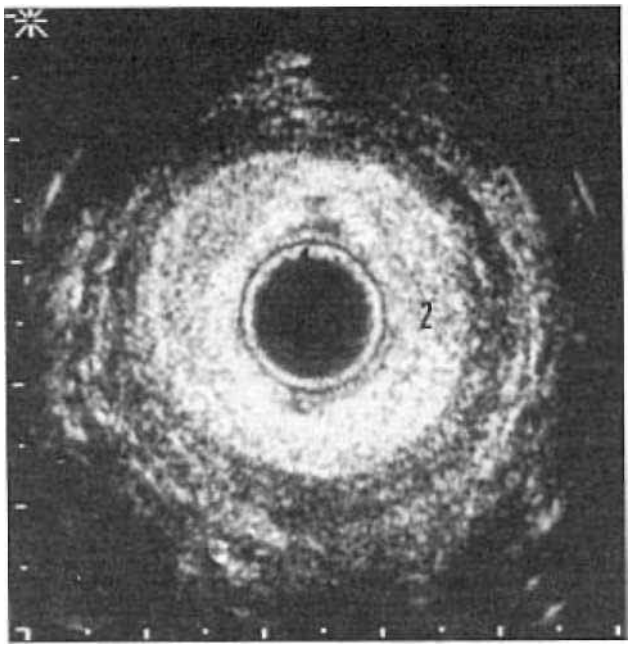

Fig. 3
Lower anal canal
1. Probe
2. Subcutaneous portion of the external anal sphincter

Anal ultrasonography in the diagnosis and management of abscess and fistula disease of the anorectum

Most anal abscesses and anal fistulas have a similar cryptoglandular origin. Infection is thought to originate in the anal glands that lie in the intesphincteric space between the internal anal sphincter and the external anal sphincter of the anal canal (7-8). Most cases of anorectal sepsis are easily cured by drainage of pus and laying open superficial fistulas. In a few patients the diagnosis of anorectal sepsis is difficult because collections of pus are deep-seated and not obvious on clinical examination.

8.5.3.1 Methodology

Endoanal ultrasound should be no more painful than digital examination of the anus. Scanning is performed at different levels by gently moving the probe in and out of the anal canal. A general examination of me anal canal is performed, looking for any obvious gaps in the sphincter muscles. Defects in the sphincter muscles may result from damage caused by sepsis (Fig 4), or follow surgical division of the sphincter and division of the sphincter by a cutting seton. Tracts and collections of pus are identified. These may lie outside the anal sphincters (Fig 5), pass through the external sphincter as a transsphincteric tract (Fig 6), or lie in the intersphincteric space (Fig 7). It can be difficult to differentiate between a tract and a small collection at one level. Both tend to be hypoechoic, but tracts often have hyperechoic shadows in the middle, which represent gas within the tract. Injecting dilute hydrogen peroxide into the external opening accentuates the interface between the fistula tract and surrounding tissues, resulting in a hyperechoic image on ultrasound scanning (2). The technique is suited particularly to recurrent fistulas.

8.5.3.2 Results

Endoanal ultrasonography using a rotating probe (10) or a linear sector probe (12) has been used for patients with Crohn's disea-

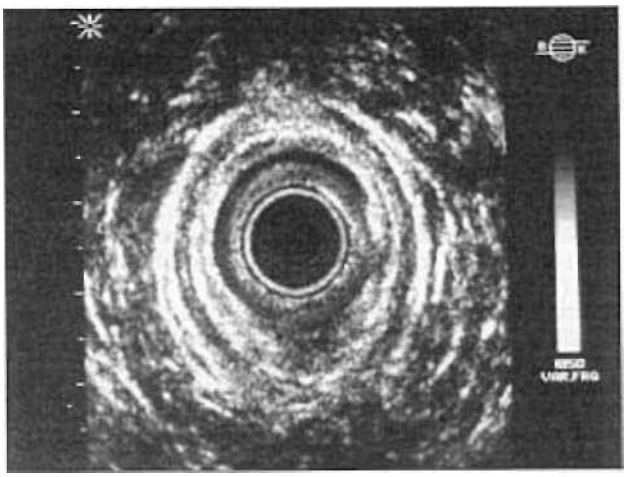

Fig.4
Fistula
Defects in the internal and external sphincter muscles at 6 o'clock may result from damage caused by sepsis

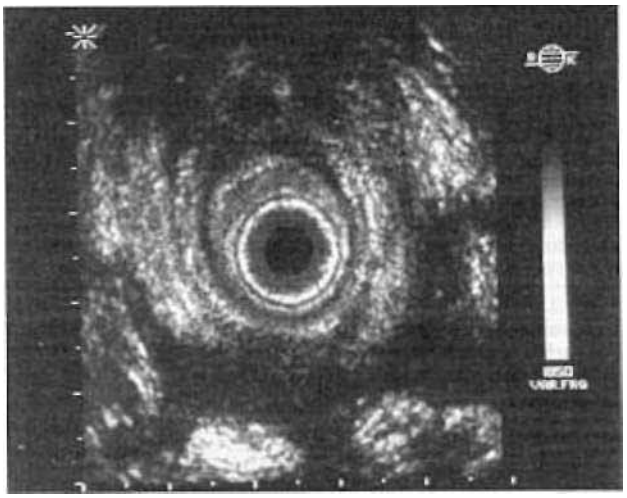

Fig. 5
Horse schoes collections of pus lying outside anal sphincters in the posterior part

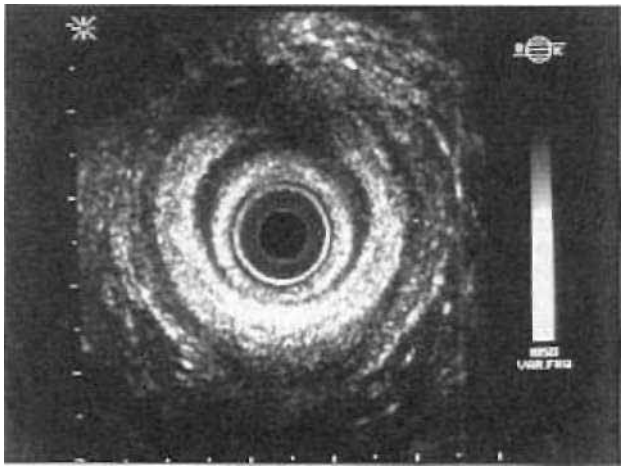

Fig. 6
Anterior transsphincteric tract, passing through the external sphincter at 12 o'clock

se, abscesses and fistulas were identified around the anal canal and lower rectum that were not detectable by clinical examination. A number of studies have been performed to examine the usefulness of endoanal ultrasound scanning in crypto-glandular and anal sepsis (3-6). Denn et al (3) reported a consecutive series of 21 patients from Birmingham with complex anal fistulas. The ultrasound findings were compared with findings at surgery. Comparison of the sonographic and surgical findings are shown in (Table 1).

A11 fistula tracts and fluid collections were identified correctly. The internal opening was difficult to indentify with confidence in most patients.

Similar results for the use of endoanal ultrasound in assessing anal fistulas were reported by the group from St Mark's Hospital (Table 2) (6).

Criteria for identifying the internal opening include a hypoechoic breach of the subepithelial layer, a defect of the internal anal sphincter and a hypoechoic lesion in the intersphincteric space. Using these new criteria, the rate of accurately identifying the site of the internal opening now is more than 80% (Fig 8).

Endoanal ultrasound scanning is useful in excluding an anal origin for sepsis in the perianal region developing from hydredenits suppurativa or a pilonidal sinus.

8.5.3.3 Conclusions

Accurate preoperative assessment of an anal fistula is fundamental for successful surgical treatment. Endoanal ultrasound provides much useful information to the surgeon.

Table 1.
Ultrasound Versus Surgical Assessment of Anal Fistulas.
Birmingham Series 7

Component	Surgery	US Right	US wrong	Accuracy
Internal opening	20	2	0	10%
Horseshoe tract	11	10	1*	91%
Fluid collection	8	8	0	100%
Fistula tracts	37	37	0	100%

Table 2.
Ultrasound Versus Surgical Assessment of Anal Fistulas.
St Mark's Series 18

A superficial horseshoe tract at the anal verge was missed b ultrasound.
Note: Results of two separate investigations into the accuracy of e n d o - inal ultrasoundf scanning in assessing anal fistulas. The ultrasouns findings were copared with the findingsa at operation.

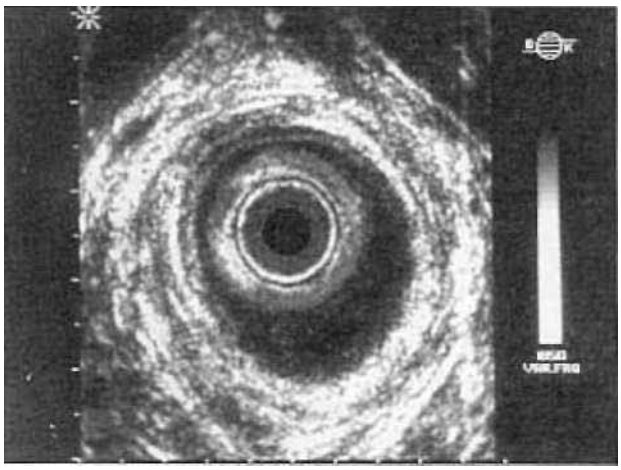

Fig. 7
Collection of pus in the intersphincteric space from 2 to 7 o'clock

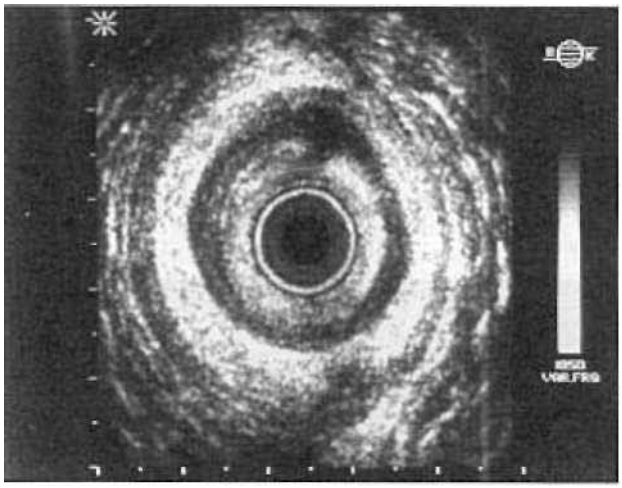

Fig. 8
Identification of 2 sites of fistula internal opening located at 12 and 6 o'clock

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TOTAL MESORECTAL EXCISION - IT'S ROLE IN RECTAL CANCER SURGERY

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Introduction: There are numerous factors, most are of technical nature, that result with different outcome of surgical intervention on the rectum. Thanks to this variety of the surgical technique McArdle an Holein Scotland found out that the local recurrence rate differs, from surgeon to surgeon, between 0 an 45% (2).
Among many other differences in the surgical techniques, a concept of Total Mesorectal Excision, seems to be accepted by most of colorectal surgeons.
This concept was first introduced by RJ Head in 1982, and was described as the main reason for low local recurrence rate.
To explain this, authors describe discontinuous spread of tumor nests into the mesorectum well distal to the lower margin of the tumor. This potential source of local recurrence led to the doctrine that total mesorectal excision should accompany anterior resection as a part of a routine procedure. Performing it in this way authors report recurrence rate lower than 5% (3). This maneuver, however, does not eradicate local recurrence, as the total rectal excision doesn't as well. It does not deal with metastatic spread in lymphnodes of the lateral pelvic wall, which is known to occur in 10 to 30%.
These data raises many dilemmas of T N M , and only multicentric randomized trial could solve them. This is however hard to achieve, since it's too difficult to standardize a precise surgical technique used by different surgeons.
It is reasonable to conclude that T N M will optimize the outcome of anterior resection by minimizing local recurrence although it will not abolish it.
As the alternative, Japanese surgeons offer their technique of extended lymphadenectomy, whereby the lateral an superior lymphatic systems are excised. This includes a high ligation of the inferior mesenteric artery and an extended periaortic and pelvic lymph node dissection beginning at the duodenum and extending down to take the periaortic and lateral iliac lymph nodes. The lateral limits of the dissection are usually the median borders of the iliac vessels, but some authors begin well out the iliac fossa wall and may even ligate the hypogastric vessels. Western colorectal surgeons remain to be convinced that the increased morbidity which is associated with extended lateral lymph node dissection jstifies the results. In addition there are similar retrospective studies which claim no benefit for the techniques (4,5).

Material and methods

From the January 1991 to the 1 of January 1997 we have operated on 286 patients with rectal carcinoma. Within all of the patients we have performed resection of the rectum and colorectal anastomosis with stapler. Of these patients, 181 were with localization of the tumor below 7cm from the anal verge, therefore we performed low and ultra-low resection of the rectum with total mesorectal excision, 96 (53%) men and 85(47%) female. Anastomosis was constructed using circular stapler or double stapling technique.

T M E technique:

Theoretical basis for practicing T M E , set by Mr. RJ Heald in so called „ T M E hypothesis" comprises two rational but as he, himself claims, unproven suppositions (6).

1. The surgical planes between the integral visceral mesentery of the hind gut and the surrounding parities provide a unique opportunity for defining a surgically achievable „tumor package".
2. By serendipity, the field of spread of rectal cancer is commonly limited to this package, i. e. the mesorectum. Its total removal encompasses virtually every tumor satelite except in cases which are already widely disseminated (7).

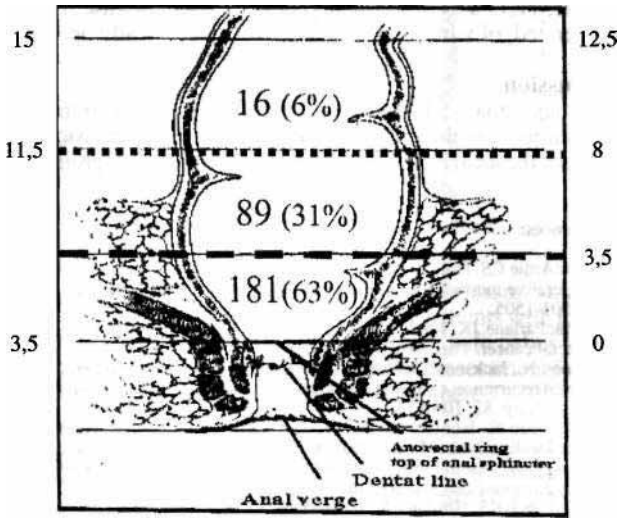
Total excision of the mesorectum is a maneuver we have reserved for the cancer of middle and lower third of the rectum, and we perform it in the original manner as Mr. Heald (8) described it only from the January 1996, till we have personally been introduced to this method by Mr. Heald (January 1996, Basingstoke) . In all other cases with localization higher then the middle third (approax. above 7cm of rectoscopic distance) we have performed transection of the mesorectum.

After separate of the left colon, high ligation of the inferior mesenteric vessels define the proximal limits of the lymphatic clearance near to the aorta. By moving downwards it is essential recognizing an avascular plane between visceral structures (rectum and mesorectum) and somatic structures (autonomic nerve plexus, sympathetic above and parasympathetic below). Sharp scissors dissection under direct vision is used throughout. Manual extraction, often performed, is to be avoided. The peritoneal incision are also widely placed and encompassed the whole peritoneal reflection. The middle rectal vessees are also divided, as far from the tumor as possible. Whether or not the sphincters are conserved, the most dangerous part of the operation is the immediate vicinity of the tumor. This is usually above pelvic floor, not involving levatore muscles. When the whole rectum with mesorectum is encompassed in this way, it can be lifted and dissected 2cm below lower margin of the tumor. In some cases when tumor permits, small reservoir of the rectum can be retain of about 2-3cm above pelvic floor. A clamp is placed across this reservoir and wash-out should be carried out. Anastomosis was performed using circular stapler or double stapling technique, depending of circumstances.
Diversion of fecal stream , by forming loop ileostomy, we found to be extreme help. It makes consequences of anastomotic leakage much easier to deal with.

Results

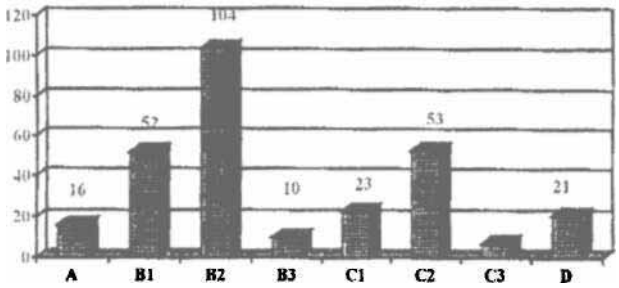
In six-year period we have treated 286 patients with rectal cancer. In all these cases we have performed anterior resection of the rectum with stapling colo recto anastomosis. Height of the anastomosis was dictated by the localization of the tumor. In 181 patient tumor was localized in the lower third of the rectum, so we performed low and ultra low anterior resection with mesorectectomy.

LEVEL OF ANASTOMOSIS



Aortoiliac lymphadenectomy and preservation of hypogastric nerves was performed in all cases. Patohistollogical findings revealed 8(4,4%)patients in A stadium of the disease, 106(58,5%) of stadium B, and 55 (30,5%) of stadium C. D stadium of the carcinoma was detected in 12 (6,6).

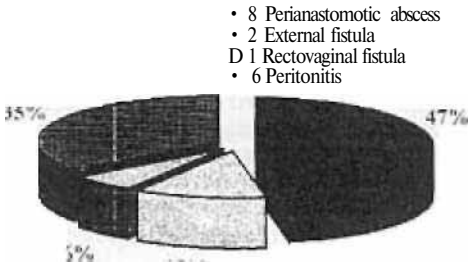
DUKES PATHOLOGICAL STAGING (Gurderson - Sosin) n-286



Loop ileostomy was as a protection to (34,8%) low and colo-anal anastomosis. T M E in it's original manner as Hr Heald had proposed it, become hanled down on our department in the 1996, after personal meeting with the surgeon. Before this we can not guarantee that the Mesorectal excision was done in the proper manner, so the results of the Total Mesorectal Excision differs till and after January 1996.

Complications connected to the anastomosis were clinically observed in 17 (5,95%). Perianostomotic abscess was noticed within 8 patients. Diffuse peritonitis occurred in 6 patients. Stercoral fistula in one and recto-vaginal fistula in one patient.

CONSEQUENCES OF ANASTOMOTIC LEAKAGE n-286



In patients with anastomoses below 7cm we had 10 anastomotic leakages which is 5,52%, while in the group with middle rectal anastomosis (7-11,5cm) we had 7 (7,86%) leakages. In group with high (more than 11,5cm) anastomosis we didn't observe signs of dehiscence. Of these 181 patinets, 6 (3,3%) died in postoperative course.

In group with low anterior resection (n-181), local recurrence was detected in 16 (9,1%) patients, local + distal recurrence in 3(1,7%) and distal in 13 patients (7,42%). Peritoneal dissemination 3 (1,71 %). Of all patients with a recurrent disease 20 were reoperated, of which 7 are cinsidered to be radically operated.

Discussion

The major goal of this series has been that the concentration by one surgeon on the technique of total mesorectal excision has reduced the local recurrence rate to 9,1 %. No control group was available but recent reports have included figures as high as 30-40%. This improvement in local recurrence has been achieved despite reduction of the mural safety margin so as to do a minimum of abdomino-perineal and permanent colostomy.

Conventional anterior resection leaves a variable amount to distal mesorectum in the pelvis: The lower tumors are not only surgically more difficult but also more closely associated with distal mesorectum than the higher one. Furthermore, varying residues of distal and perirectal lympho-vascular tissue could explain the enormous variations in reported local recurrence rates after different operations reported from different surgeons. Enker (9) and colleagues from Sloan Ketering Cancer Center found a local recurrence rate of 7,3% in a consecutive series 246 patients with rectal cancer treated by T M E. This recurrence rate included both patients with and without distant metastases and was considered to be significantly better. In Mc Call et al's review of the literature the median local recurrence rate was 18,5% after follow up in 10465 patients (10). Of these patients, 1022 had undergone T M E. The local recurrence rate in those undergone T N E was 7,1%. It does appear therefore that T M E holds the promise of considerable reducing local recurrence but attention to detail will be required to prevent complications. Provided the anatomy of the pelvic nerves are understood, bladder and sexual dysfunction should be avoided. Readers are refered to an excellent review of this anatomy by Havenga et all (11,12).

One concern that has been is that T M E may lead to a high incidence of anastomotic dehiscence. Thus in Heald's series (13) there were 24 (11 %) major anastomotic leaks in 219 patients undergoing low sphincter saving resection with T M E. In addition further 14 (6,4%) of asymtomatic leaks were found on contrast enemas. It may be that T M E results in the devascularization of the anorectal stump. For this reason a defunctioning stoma has been recommended as a routine addition when T M E is used (14).

On the other hand Japanese authors understand T M E little bit different than most Western surgeons, especially Scandinavians. As Mr. Takahashi states that Mr. Heald's term „Holly plane" does not exist as an anatomical term but a technical one, and that lymphonodectomy should not remain within these borders, but extend to outer tissue surrounding internal iliac vessels (second and third space). According to Mr. Takahashi, mesorectum is set only for the first space, and he gives a number of 125 of 1136 cases, of positive nodes outside mesorectum (15).

However this question remains open for further debates.

Conclusion

As the essence of this paper we can stress out the claim that Total Mesorectal Excision should become the defined objective of rectal cancer surgery, that nerve visualization and preservation should be possible in most cases, and that the anal sphincters need to be sacrificed in no more than 15% of patients. „There is no area of treatment where the development of better surgical technique has so much to offer the patient" - R. J. Heald.

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FUNCTION PRESERVING OPERATION FOR RECTAL CANCER BASED ON PREOPERATIVE STAGING BY ENDORECTAL EUS AND MRI BY TWO OBLIQUE METHOD

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Background

The significance of intrapelvic lymphadenectomy has been confirmed in rectal cancer surgery in Japan (1). Patients with rectal cancer, who received intrapelvic lymphadenectomy, may obtain better long-term survival after operation, but may have the urinary and sexual dysfuction caused by the injury of pelvic nerves at operation (2-4).

Preoperative staging, which is synthesized from various kinds of imagings including endorectal ultrasonography (EUS), computed tomography (CT), and magnetic resonance imaging (MRI) (5, 6), is very important in order to perform both operative curativity and postoperative quality of life (QOL).

It has been generally accepted that the incidence of intrapelvic lymphnode metastases depends upon tumor location and tumor depth. Tumor location can be easily defined by digital examination, barium enema or colonoscopy. The preoperative accuracy of tumor depth has also been improved by the development of endorectal EUS. The present problem may be how EUS assessment for tumor depth is applied to the determination of operation method of rectal cancer.

On the other hand, the identification of intrapelvic lymphnodes including the anatomical correlation with the branches of internal iliac artery is yet poor, and so the intrapelvic lymphnode dissection may be insufficient at operation. The blind extended intrapelvic lymphadenectomy, which injures the feeding vessels of pelvic organ and muscles, would decrease postoperative QOL of patients including the urinary or sexual dysfunction.

The present problem about the surgical treatment for rectal cancer is described from curativity and QOL based on our results. It has been investigated whether preoperative endorectal EUS and MRI of the pelvic cavity is significant or not in order to decide the indication for intrapelvic lymphadenectomy and perform an operation with more sufficient curativity and QOL.

Materials and Methods

From 1987 to 1997, 154 patients with rectal cancer received curative operation in the Second Department of surgery, Wakayama Medical School in Japan. Rectal cancer was classified into upper cancer (n=74: above 8 cm from anus), middle cancer (n=38: 5-8 cm) and lower cancer (n=38: below 5 cm) according to the distance from anal verge to the lower margin of tumor on preoperative colonoscopy.

Preoperatively, endorectal EUS was performed for 115 patients without tumor stenosis using Olympus CF-UM20 (radial scanning probe, 7.5 MHz transducer) after cleasing the colonic lumen with 2,000 ml of peroral polyethylene glycol solution. EUS was performed as follows. Rectal lumen was filled with deaerated water. A thin rubber sheath, which was placed over the transducer, was filled with about 50 ml of water Tumor depth was assessed according to the Mucosal (M; T1), the Submucosal (SM; T1), the Muscularis proprial (MP; T2), the Adventitial (A; T3) or Serosal (S; T3) invasion, and the tumor penetration into surrounding organs (Ai; T4). EUS assessment was compared with postoperative pathological tumor depth, and the accuracy of the examination was determined.

The application of EUS assessment for rectal cancer surgery is as follows. Patients with upper rectal cancer did not receive intrapelvic lymphadenectomy irrespective of tumor depth, although the upper lymphatic route along inferior mesenteric artery was dissected completely. Patients, who had middle rectal cancer with A (S) invasion or lower rectal cancer with MP of A (S) invasion on EUS, received intrapelvic lymphadenectomy as well as upper route lymphadenectomy. The incidence of lymphnode metastasis was compared among three groups.

Postoperative intrapelvic local recurrence was examined according to tumor location or depth of primary rectal cancer, and the extent of lymphnode metastasis at operation. Postoperative survival was compared among upper, middle and lower rectal cancer.

Since 1996, MRI imaging of the pelvic cavity has been performed for 41 patients by two oblique method using Hitachi MRH 500AD. It was aimed to detect intrapelvic lymphnode swelling correlating anatomically with the branches of the internal iliac artery. MRI by two oblique method, which was scanned with Tl weighted images of 12 slices every 8 mm, was performed on coronal oblique dimension connecting pubic tubercle and crista obturatoria, and on saggital oblique dimension with a 10 degree slope scanning from the saggital line (Figure 1).

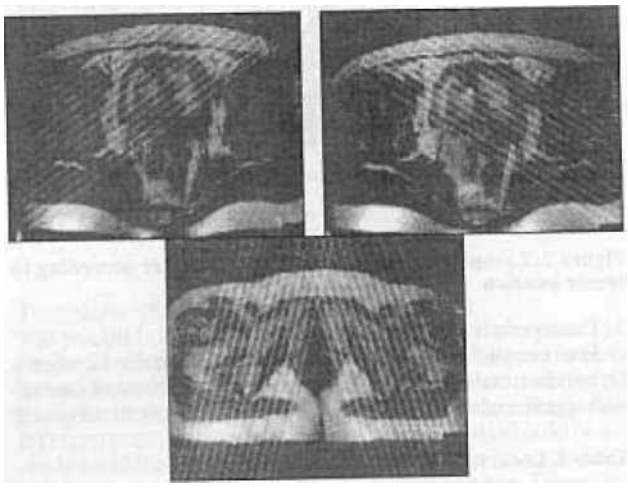


Figure 1. Preoperative MRI by two oblique method

After the introduction of preoperative MRI assessment, complete intrapelvic lymphadenectomy for the patients with middle or lower rectal cancer has been performed with pelvic autonomic nerve preserving. Preoperative MRI assessment for the intrapelvic lymphnode metastasis was compared with postoperative pathological findings.

Postoperative urinary disturbances, as an indicator of the postoperative QOL, were examined from 54 patients, composed of 21 with complete pelvic nerve preserving at operation and 33 with partial preserving or non-preserving. The degree of disturbances was divided into no disturbance, moderate disturbance (prolonged of urination, sense of residual urine), and self-catheterization.

Results

1. Accuracy of tumor depth by preoperative endorectal EUS (Table 1)

The overall accuracy of endorectal EUS was 77.4% (T1: 80.0%, T2:64.3%, T3:82.3%, T4:25.0%), with 16.5%(19patients) overstaged and 7.1% (7 patients) understaged. Of 14 patients with T2 invasion on EUS, 14.3% was overstaged and 21.4% was understaged. Of 79 patients with T3 invasion on EUS, 16.5% was overstaged and only 1.3% was understaged.

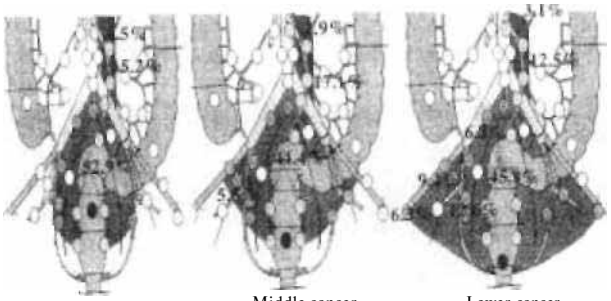
Table 1. Accuracy of endorectal EUS for the depth invasion of rectal cancer

		Pathological findings					Total	Accuracy
		Early cancer		Advanced cancer				
		m	sm	mp	a	ai		
EUS	(M)	6*	1	1			8	75.0%
	T1 (SM)	1	8*	1			10	80.0%
	T2 (MP)		2	9*	3		14	64.3%
	T3 (A)		2	11	65*	1	79	82.3%
	T4 (Ai)			1	2	1*	4	25.0%
	Total	7	13	23	70	2	115	77.4%

* accurate diagnosis

2. Lymphnode metastasis according to tumor location of rectal cancer (Figure 2)

The incidence of the lymphnode metastasis was 52.9% along the upper route in upper rectal cancer. It was 44.4% along the upper lymphatic route, and 5.8% along the intrapelvic route in middle rectal cancer. It was 45.9%, and 18.9% in lower rectal cancer, respectively.



Upper cancer (n=74) | Middle cancer (n=42) | Lower cancer (n=38)

Figure 2. Lymphnode metastasis of rectal cancer according to tumor location

3. Postoperative local recurrence (Table 2)

Postoperative intrapelvic local recurrence appeared in 12 patients (1; middle rectal cancer, 11; lower rectal cancer). None of patients with upper rectal cancer had local recurrence. In 11 patients withlower rectal cancer, pathological tumor depth, which was showed mp invasion in two patients (EUS accuracy: 50%) and adventitial invasion in ten patients (EUS accuracy: 100%). It occurred in only one (2.3%) of 43 patients who had no lymphnode metastasis in middle and lower rectal cancers at operation. It was showed retrospectively that 11 (91.7%) patients had had lymphnode metastases along the upper route, and 6 (50.0%) along the intrapelvic route at operation.

Table 2. Local recurrence of rectal cancer

Location of cancer	Patient (age, sex)	Preoperation Tumor location	EUS	MRI	Operation	Postoperative findings Tumor depth	Node	metastasis upper	Dukes intrapelvic		Recurrence (mo)
Middle	1) 76 M	6	A		APR	a	(+)	(–)	C		38
	2) 52 F	6 cm	A**		APR*	a**	(+)	(–)	C		24
	3) 76 M	5	MP***		APR	mp***	(+)	(+)	C		6
	4) 60 F	5	A		APR	mp	(–)	(–)	B		28
	5) 76 F	5	A		APR	a	(+)	(+)	C		11
	6) 71 M	5	A		APR	a	(+)	(–)	C		30
Lower	7) 38 M	4	A		APR	a	(+)	(+)	C		24
	8) 62 M	2	A		APR	a	(+)	(+)	C		20
	9) 43 F	3	A		APR	a	(+)	(–)	C		65
	10) 41 F	3	A		APR	a	(+)	(–)	C		9
	11) 62 M	5	A	(–)	APR	a	(+)	(–)	C		12
	12) 64 M	5	A	(–)	APR	a	(+)	(+)	C		28

APR* abdomino-perineal resection ** Adventitial layer *** Muscularis proprial layer

4. Postoperative survival (Figure 3)

Postoperative cumulative 5-year survival was significantly lower ($p<0.05$) in patients with lower rectal cancer (57.7%) than those with upper rectal cancer (68.3%) and those with middle rectal cancer (73.3%).

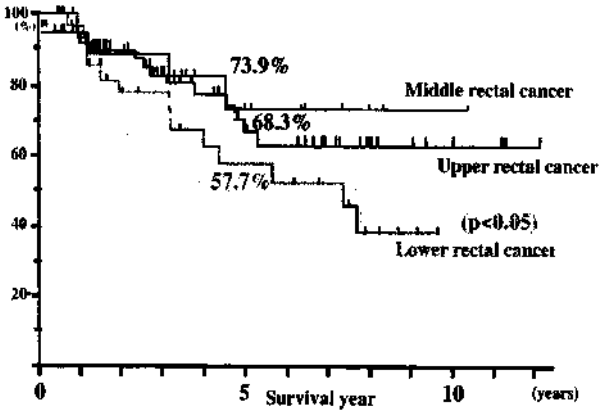


Figure 3. Postoperative survival of rectal cancer according to tumor location

5. Accuracy of intrapelvic lymphnode metastasis with MRI by two oblique method

Preoperative **MRI** imaging by two oblique method has been aimed for the complete dissection of intrapelvic lymphnodes. It could reveal the branches of internal iliac artery, including superior gluteal artery, superior vesical artery, obturator artery, inferior gluteal artery and internal pudendal artery. Particularly, sagittal oblique dimension showed the region around inferior gluteal artey, middle rectal artery, and internal pudendal artery near the pelvic plexus.

Postoperative pathological diagnosis was compared with preoperative MRI assessment. Overall accuracy was 90.2%. Positive sensitivity was 60.0% (3/5). The sensitivity was the highest for the lymphnode metastases along middle rectal artery, although it was poor for those in obturator space. Less than 5 mm sized metastaticlymphnodes was showed to have been false-negative on preoperative MRI.

6. Postoperative urinary disturbances

Of 21 patients with complete pelvic nerve preserving at operation, 18 (85.7%) had no urinary disturbances, and none needed self-catheterization. Of 33 patients who received extended intrapelvic lymphadenectomy with partial pelvic nerve preserving or non-preserving, 6 (18.2%) needed self-catheterization.

Discussion

Local failure and urinary and sexual dysfunction after rectal cancer surgery remains unsolved (7), although some of new treatments have been introduced in recent years. In many Europien countries and the USA, preoperative radiation therapy and total mesorectal excision (TME) (8-10) at operation seems to be confirmed to achieve good local control.

On the other hand, in Japan, complete intrapelvic lymphadenectomy was performed in 1980's including the resection of pelvic autonomic nerves (1,4). It improved postoperative survival rate, but invited urinary and sexual dysfunction. At present, pelvic autonomic-nerve preserving operation (11,12) is the main current in the operation of advanced rectal cancer whether intrapelvic lymphadenectomy is performed or not.

Whether surgical treatment for rectal cancer can satisfy both curativity and postoperative QOL of patients or not depends wholly upon preoperative staging of cancer.

Tumor location is one of the important factors to determine the indication for intrapelvic lymphadenectomy. As tumor location lowered near the anal verge, the incidence of intrapelvic lymphnode metastasis increased. Patients with upper rectal cancer did not have local recurrence although they did not receive intrapelvic lymphadenectomy. Patients with middle rectal cancer had satisfactory survival after the conventional operation with intrapelvic lymphadenectomy, according to preoperative staging based on endorectal EUS assessment.

But, patients with lower rectal cancer existing within 5 cm from the anal verge had sometimes local recurrence postoperatively. Local recurrence occurred in patients who had received rectal amputation accompanied with total mesorectal excison. Considering that 10 (90.9%) of 11 patients were Dukes C including 6 (54.5%) patients with intrapelvic lymphnode metastasis, and that a period from operation to local recurrence was within 24 months in 7 (58.3%) of 12 patients, it is suggested that local control at operation was insufficient.

MRI imaging of the pelvic cavity by two oblique method has enabled us to reveal the anatomy of the branches of internal iliac artery, including superior gluteal artery, superior vesical artery, obturator artery, inferior gluteal artery and internal pudendal artery. Preoperative imaging of the branches of internal iliac artery and lymphnode swelling was very useful to perform more complete intrapelvic lymphadenectomy with the preserving of pelvic nerves and vessels. The lymphnode along middle rectal artery, which exists near the pelvic plexus, has the highest incidence of metastasis in patients with lower rectal cancer. The sagittal oblique assessment of MRI gave good sensitivity for that lymphnode. The size of the lymphnode is responsible for the detection with MRI (13). Less than 5 mm sized metastatic lymphnodes in obturator space could not be detected in this study. It is only three years since MRI imaging was introduced for preoperative staging of rectal cancer.

It was showed in our recent study that pelvic autonomic nerve preserving operation decreased postoperative urinary disturbances. In the future, the decrease of postoperative local recurrence and the improvement of survival in lower rectal cancer is expected.

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ULTRASOUND STAGING OF RECTAL TUMOURS

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Introduction: A variety of surgical options are nowadays available in the treatment of patients with rectal cancers (1,4,9). The choice of treatment depends on the height of tumor from the anal verge, the stage, the presence of lymph nodes, the differenciation, the presence of synchronous lesions, the nature of the underlying pathology. Local treatment by surgical excision or local radiotherapy for early cancer requires precise identification of cases suitable for such treatment without risk of increased long term mortality.

Digital assessment is limited to tumours located within 8 to 10 cm of the anal margin and gives information only on the height, size and fixity of the lesion but doesn't provide with accurate data on the degree of wall penetration nor on the presence of pararectal lymph nodes involvement. Studies of Mason (21) and Nicholls (25) report a 75 % accuracy in predicting pathological state. More recent data show that the digital examination is particularly poor in early lesions (5,28). Need for more accurate investigations is necessary and explains the increasing interest for endorectal ultrasonography.

Ultrasonography is an imaging technique whose principle is based on the interaction between transmitted sound waves and the juxtaposed different tissue densities of the body.

Ultrasonography is less expensive, relatively quick and is well tolerated by the patient. Moreover, the patient is not exposed to radiation during the course of the examination.

The development of rotating probes allows real-time 360° radial scanning of the anorectum and the surrounding structures. Among many other applications, preoperative staging of rectal cancers has gain more and more clinical importance.

Technique of Endorectal Ultrasonography

The patient is instructed to prepare his bowel with one or two Fleet enemas 1 hour before the examination. There is no need for sedation, and therefore no need for specialised monitoring. The patient is placed in the gynecologic position. With digital rectal examination a significant anal stenosis should be excluded and the anal canal lubricated.

We currently use the 1846 Bruel & Kjaer (Naerum, Denmark) scanner and a 7.0 MHz 8539 transducer with a focal length of 2 to 5 cm. A small finger cot balloon is placed over the transducer and properly secured in place. The probe is introduced through the anus or passed through a short rectoscope in order to reach the upper part of the rectum and be placed in the proper position in front of the identified rectal lesion.The balloon is distended with water. Any bubble should be eliminated. By convention, the ultrasound probe is held with the spigot in the upright position, and the probe is maintained in the centre of the lumen.

Technical pitfalls (18) in ERUS include proximity of the lesion to the anal verge, improper balloon inflation, a non perpendicular imaging plane, shadowing artifacts due to air or stool, reverberation artifacts, refraction artifacts and a transducer gain setting that is too high.

After a more or less long learning curve and increasing experience of the examinator these artifacts can be identified or prevented and diagnosis accuracy increased.

Normal endorectal ultrasonography (E R U S) image

The normal rectal wall is represented by concentric circles of alternating hyperechoic and hypoechoic bands. The majority of investigators agree on a 5-layer model of the rectal wall (Fig 1), although there is some disagreement on the anatomic correlation of each of these lines (Table 1). Hildebrandt et al (11) believe that the three white lines represent interfaces, whereas the inner dark lines represent actual anatomic layers. In this model, the first white line is the interface between the balloon and the mucosa. The first dark line represents both the mucosa and the submucosa, which is followed by the middle white line, which they feel represents the interface between the submucosa and the muscularis propria: The outer dark line represents the muscularis propria followed by the interface with the perirectal fat, the outer white line.

Table 1. Interpretation of the Anatomic Correlation of the 5-Layer Rectal Wall Model

Series	Line 1	Line 2	Line3	Line 4	Line 5 "
	(White)	(Dark)	(White)	(Dark)	(White)
Hildebrandt et al 11	Interface (balloon/ mucosa)	Mucosa/ submucosa	Interface (submucosa /muscularis propria)	Muscularis propria	Interface (rectal wall/perirectal fat
Beynon et al 2	Interface (balloon/ mucosa	Mucosa/ muscularis mucosa	Submucosa	Muscularis propna	Perirectal fat
Saitoh et al 31	Interface (balloon/ mucosa)	Mucosa	Submucosa	Muscularis propria	Perirectal fat

Preoperative Staging of Rectal Neoplasm With Endorectal Ultrasonography

The crucial layer is the middle white line, which, if broken, implies invasion through the muscularis mucosa into the submucosa (T1). If there is widening of the outer dark line, but no break in the outer white line, then the tumour is confined to the muscularis propria (T2), and if there is a break in the outer white line, the tumour has invaded the perirectal fat (T3).

In order to correlate US datas with T N M pathological findings, E R U S observations are quoted U T 1, U T 2, U T 3 and U T 4 (Table 2).

Table 2.

	Ultrasonic stage	Clinical stage
	Tumour confined to submucosa	Tumour 2 cm or less in greatest dimension
	Tumour invades muscle	Tumour larger than 2 cm but not more than 5 cm
	Tumour involves perirectal fat	Tumour larger than 5 cm in greatest dimension
T4	Tumour invades adjacent organ	Tumour involves adjacent organ

UT1 Lesion: Confined to Submucosa

If the middle white line (submucosa) seen on E R U S is broken by a malignant lesion, this corresponds to submucosal invasion. The lesion is said to be confined to the submucosa and is hence a U T 1 tumour.

The reported incidence of lymph node metastases in such a lesion varies from 6% to 11%.
(9-24).

UT2 Lesion: Involving Muscularis Propria but Confined to Bowel Wall

Breach of the middle white line with expansion of the outer black line (muscularis propria) but preservation of the outer white line (perirectal fat) constitutes a U T 2 lesion.

The incidence of regional lymph node involvement is between 10% and 35% (31-33) when the muscularis propria is involved.

UT3 Lesion: invasion into Perirectal Fat

When the outermost white line (perirectal fat) is broken, often by a hypoechoic irregular extension of a tumour, into perirectal fat the lesion described a U T 3.

UT4 Lesion

Invasion of adjacent organs constitutes a U T 4 lesion. It is possible to visualise several structures in close proximity to the rectum by ultrasound. In women, the vagina, uterus, and bladder may be visualised. In men, interruption of Denonvilliers fascia (a white line between the rectum and the prostate gland and seminal vesicles) suggests tumor extension into these structures.

In man the seminal vesicles are clearly observed and must be distinguished from lymph nodes. The prostate is also clearly observed, and any tumor invasion through Denonvillier's fascia can be easily recognised.

Lymph nodes

The ultrasound allows visualisation of the immediate perirectal tissue, and therefore a search for enlarged lymph nodes should be a routine step in the evaluation of a rectal tumour. One must be careful not to confuse blood vessels with enlarged lymph nodes.

Only a minority of lymph nodes are detected by E R U S. Detry et coll (7) could demonstrate by preoperative E R U S correlated with anatomical studies of operative specimens that detection of lymph nodes increases with their size: 12,8 % of the 3 to 5 mm nodes, 43.4 % of 6 to 10 mm nodes and 85.7 % of over 10 mm nodes. Metastatic lymph nodes are reported as having a hypoechogenic appearance. Metastatic and non metastatic lymph nodes exhibit a great variety of morphological features and it is difficult to reliably correlate a specific appearance with invasion. An enlarged lymph node located adjacent or superior to the level of the tumour, having a round appearance with sharp border, and of the same hypoechoic echogenicity as the primary tumour should be considered as a metastatic node (12).

The differentiation between an inflammatory node versus a metastatic one can be difficult and their size is of little value in differentiating them (3).

Table 3. Comparison of Lymph Node Staging

Author	Year	Number	Accuracy	Sensitivity	Specificity	PPV	NPV
Holdsworth 13	1988	36	61%	59%	64%	50%	70%
Beynon 3	1989	95	83%	88%	79%	78%	89%
Milsom 22	1993	61	77%	64%	87%	74%	81%
Herzog 10	1993	111	80%	89%	73%	71%	90%
Solomon 32	1993	517	58%	79%	80%	74%	84%
Deen 6	1993	106	77%	68%	84%	68%	83%

In published series (Tabl 3) comparing E R U S and histopathology the ability of sonography to assess non-involved nodes - specificity- range from 64 % to 87 %. The sensitivity or ability to predict lymph nodes metastasis range from 59 % to 88 %. The accuracy or ability of E R U S to predict involved and non-involved nodes range from 61 % to 83 %. Evaluation of lymph node involvement is still an important weakness of E R U S.

Improvement could be achieved by ultrasound-guided biopsies of enlarged lymph nodes (23) but further evaluation is necessary.

Benign Villous Adenoma.

Villous adenoma that appears benign on clinical examination may include carcinomatous changes in 9 % to 42 % (26,27). Random biopsies are not representative and excisional biopsy of the whole lesion may require a subsquent procedure in case of malignant changes.

Using E R U S, a reliable preoperative assessment of malignant change in large villous lesions may be obtained thus helping to plan definitive treatment.

The middle white line (hyperechoic) seen on ultrasound is the

key to diagnose a benign lesion. This line corresponds to the submucosa and, if intact ascertains that no invasive malignancy is present: the lesion is quoted UTO. An invasive tumor is when malignancy has extended beyond the muscularis mucosae and into the submucosa crossing the white line on ERUS.

Results

ERUS correlated with pathological examination of operative specimens shows a high accuracy, ranging from 80 to 92 %, in evaluating the depth of rectal wall penetration (Tabl 4).

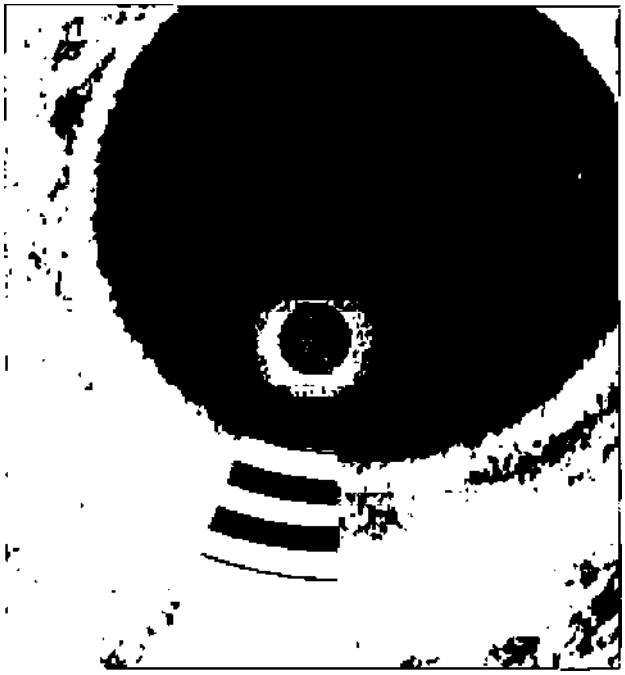
Table 4. Comparison of Depth of Wall Penetration Using ERUS

Author	Year	Patients	Accuracy	Overstaged	Understaged
Hildebrandt 11	1986	76	88%	11%	9%
Beynon 2	1987	49	90%	6%	4%
Holds worth 13	1988	36	86%	11%	3%
Zainea 35	1989	30	90%	3%	7%
Katsura 17	1992	120	92%	4%	4%
Lindmark 20	1992	63	81%	8%	8%
Milsom 22	1993	67	85%	12%	3%
Herzog 10	1993	118	89%	10%	1%
Deen6	1993	209	82%	12%	2%
Garetti 16	1997	58	80%	27%	8%

Overstaging is observed in 3 to 12% of cases mainly in UT3 / PT2 tumors. This is due to difficult evaluation of tumours just penetrating into the muscularis propria from penetration through the whole thickness of the muscularis propria. Furthermore, overstaging may be due to inflammation -spontaneous or iatrogenic- around a tumour which results in a hypoechogenic appearance, and from reaction or retraction of the muscularis propria in the neighbourgh of a tumour (6,15).
With ERUS benign villous tumours can be distinguished from lesions presenting malignant changes (26,27) and adequat treatment selected (30).
ERUS allows identification of small carcinoma with a low risk of lymph node involvement suitable for local excision .In case of larger tumours, precise staging helps in decision making about operative strategy and need for preoperative radiotherapy (30).
ERUS offers also a method for assessing degree of shrinkage and downstaging of UT3 and UT4 lesions after radio-chemotherapy (34). Better criteria should still be developped to distinguish tumour remnant from radiation induced changes to perirectal tissues. Our ability to assess local eradication of rectal cancer following radiation therapy remains poor.
ERUS has also been used postoperatively to identify locally recurrent rectal cancer at an early and potentially curable stage. 62 patients enrolled in a prospective study (29): 11 cases developped a local recurrence which has been suggested or identified by ERUS in all cases and not by other techniques.
New promissing development are under evaluation. Three-dimensional endosonography enhance the diagnostic accuracy (14,16). Even stenotic rectal cancers could be staged. With 3D-sonography compared with conventional ERUS, Hunerbein (14) could demonstrate an increase in accuracy in the assessment of infiltration depth from 82 % to 88 % and in accuracy in node involvement from 74 % to 79 %. In the future, three dimensional ERUS will also be useful to reconstruct tumours and to optimize the radiation target geometry.

Fig.11.The majority of investigators agree on a 5-layer model of **the rectal wall:**

1. The first white line is the interface between the balloon and the mucosa
2. The first dark line represents both the mucosa and the submucosa
3. The middle white line, interface between the submucosa and the muscularis propria
4. Outer dark line muscularis propria
5. Outer white line interface with the perirectal fat



Conclusion

Endorectal ultrasound enables invasion between neoplasm confined to the mucosa and those that invade submucosa. Of invasive tumours, those confined to the submucosa (T1) are ideally suited to local excision, whereas some lesions which involve muscularis propria but do not penetrate this layer (T2) may also be suitable for local therapy. The technique is reliable in experienced hands and may change the management of patients with early cancers more than in patients with advanced cancer (32). It is a better predictor of wall invasion and para-rectal lymph node involvement compared with CT (35). However, further studies are required to assess the accuracy of ultrasound in comparison with MRI. Thus, in 1999, endorectal ultrasound remains the method of choice in preoperative assessment of patients with rectal neoplasm and in postoperative follow-up.

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ULTRASOUND STAGING OF THE RECTAL CARCINOMA

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Summary: Author presents his own thirteen years lasting experiences in using of Endoanal Transrectal Ultrasonography (ET USG). In accordance with more than 3300 examinations he proves accuracy, easy using and inevitability of ET USG in pre-operative determination of the rectal carcinoma staging. In post-operative observing author emphasises the meaning of ET USG for early determination of local recurrences of the rectal carcinomas, that enables to indicate "second look" operative performances as soon as possible.
Author points at the possible using of the ET USG by the evaluation of the continuity in the sphincter apparatus of the rectum as well as in diagnostics of the periproctal fistulas and abscesses.
Key words: endoanal transrectal ultrasonography, rectal carcinoma

Introduction

Digital examination of the rectum, endoscopic examination, determination of the C E A and Ca 19-9 levels, irrigoscopic examination, CT and MR have inevitable place in the diagnostics of the rectal carcinomas (sheet 1). Besides the CT and MR there is not possible to determine the staging of the rectal tumours one from the decisive factors of the operative modalities selection. CT and MR are able to diagnose just tumours in the size of more than 2 cm and besides both me-thods are quite costly. (5,9). Using of ET U S G in the clinical practice means a revolution in the early anatomic diagnostics of the rectal tumours. ET U S G enables to diagnose also the tumours in the size of less than 2 cm. (4,10,11). It enables to determine the extent of the tumour infiltration in separate re-ctal stratums, in lymph nodes in the meso-rectum, in perire-ctal tissue and as well as possible infiltration of the organs close to the rectum. (Sheet 2).

Material and methods

At our Surgical Department we work with the Brüel & Kjaer sonographic device, type 1846, with the endosonic probe of 7 M H z, type 1850. The probe is 24 cm long and its diameter is 19 mm. There is a taking off equipment on the probeis end and this rotates in the water environment. The head rotates 6 times in a second and U S G signal is received in angle of 90 degrees measured from the axis and continuously the

Sheet 1: Diagnostics of the rectal tumours

1 Digital examination - criterions according to Mason
2 Endoscopic examination
3 Endoanal transrectal Ultrasonography
4 Determination of C E A and Ca 19-9 levels
5 Irrigoscopic examination
6 CT
7 M R

Sheet 2: Using of ET U S G in surgery

Pre-operative

1 Diagnostics of rectal tumours
2 Determination of rectal tumours staging
3 Determination of lymph nodes involvement in mesorectum
4 Determination of the infiltration extent in perirectal tissue and closed organs
5 Diagnostics of the periproctal abscesses and fistulas
6 Judgement of the continuity of puborectal sling and sphincter apparatus of the rectum

Post-operative

1 Diagnostics of local recurrences of rectal carcinomas after the sphincter saving operations
2 Diagnostics of local recurrences after the operations according to Miles by women

360 degrees transversal sonographic cut of the rectum is created. Such cut enables to differentiate 5 basic stratums of the rectal wall: two hyper-echogenic zones - submucosa and serosa, and three hypo-echogenic zones - mucosa, muscularis mucosae and muscularis propria. (Picture 1).

ET U S G enables the pre-operative verification of four levels in tumour infiltration of the rectal wall, perirectal tissue and closed organs:

Sheet 3: ET USG - set of 3324 examinations (1.1.1986-31.12.1998)

Examinations	*Number*
Malignant and benign tumours of the rectum	512
Post-operative transrectal examinations	1642
Post-operative transvaginal examinations	146
Judgement of the gynaecological tumours involvement in the pelvis	324
Periproctal abscesses and fistulas	348
Examination of the continent apparatus of the rectum	352

Sheet 4: Observed parameters and frequention of the examinations in post-operative period

Type of examination	*1 month after operation*	*Every 3 months after operation*
Clinical examination	+	+
Endoanal transrectal USG	+	+
USG of the liver	+	+
CEA, Ca 19-9	+	+
Endoscopy	+	+
X-ray of the lungs	+	+
CT and/or MR	In the case of doubts about ET USG finding	

Sheet 5: Indications for "second look" operations

1 In the dynamic pursuing increased C E A or Ca 19-9
2 Positive finding of the recurrence by the ET USG
3 Positive finding by endoscopic examination in the correlation with the histologic examination of the taken biopsy
4 Positive finding of the recurrence by the CT or MR in the correlation with items 1 and 2

Sheet 6: Strengths and disadvantages of ET USG in surgery

Strengths

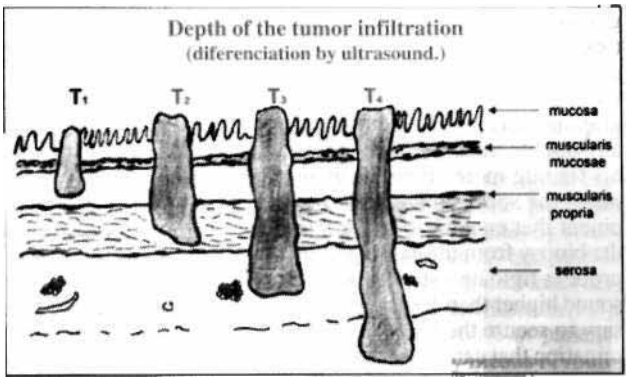
1 Examination makes any stress for patient
2 Simple manipulation with the endoprobe and equipment
3 Excellent precognitive ability of the device
4 Clear interpretation of taken sonographic cut of the rectum
5 Possibility to diagnose rectal tumours in size less than 2 cm
6 Economic advantage

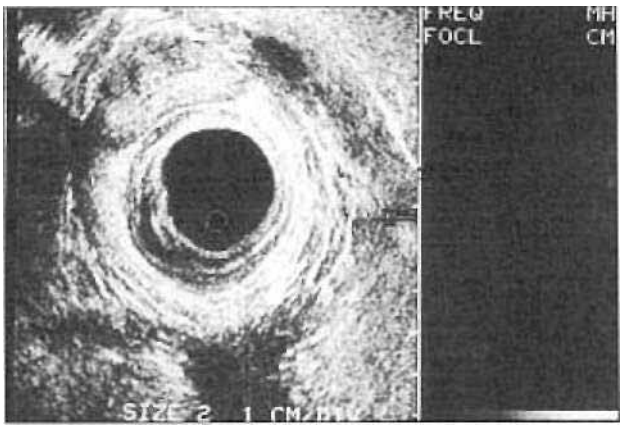
Disadvantage

1 Diameter of the rectum have to be more than 2 cm
2 Rigid handle of the endosonic probe

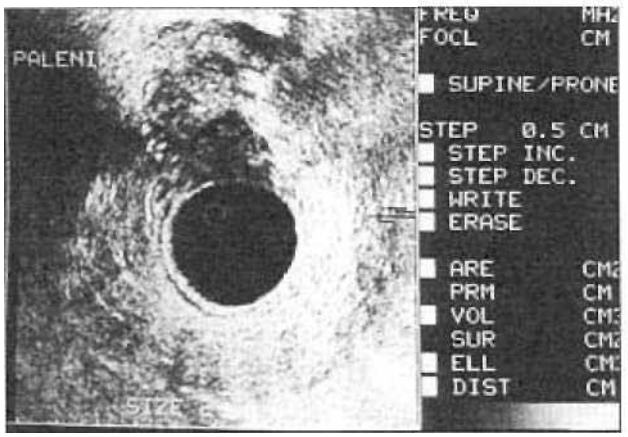
T1 - tumour infiltrates the mucosa and submucosa (picture 2)
T2 - tumour infiltrates the rectal wallis musculans to serosa (picture 3)
T3 - tumour penetrates through serosa to the perirectal tissue (picture 4)
T4 - tumour infiltrates the closed organs (picture 5)

Picture 1: Depth of the tumour infiltration



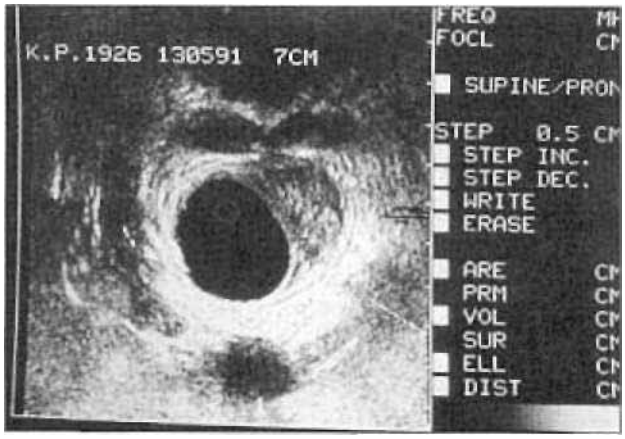


Picture 2: Rectal tumour in the stage uT_1

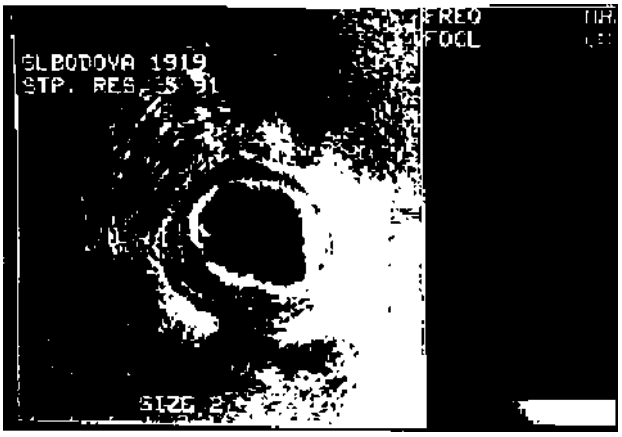


Picture 3: Rectal tumour in the stage uT_2

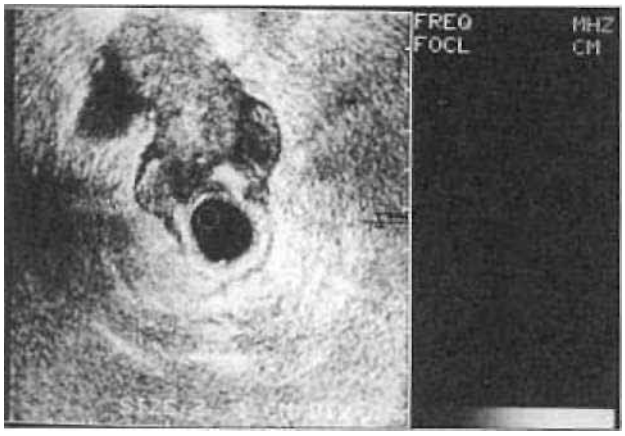
ET USG enables the precise evaluation of the mesorectal lymph nodes' status and the precise determination of their size, location and number. (5,6,10)
I made 3 324 ET U S G examinations from January 1 st, 1986 to December 31 st, 1998 and I examined 512 patients with malignant and benign rectal tumours. In post-operative period, during the regular ET U S G controls of every 3 months, I made 1642 examinations. I made trans-vaginal examination by 146 patients and 324 ET U S G controls by the verification of the gynaecological tumours" possible invasivity. For the indication of the perirectal space inflammative affections I made 348 examinations. I judged the continent apparatus of the rectum and continuity of m. puborectalis by 342 patients. (Sheet 3).
We have a computerised Dispensary of the malignant diseases of colon and rectum with the list of the patients after the sphincter saving operations for the low-sided rectal carcinomas in our Department. Every three months are these patients examined with using of ET U S G and contemporaneously besides other parameters we observe also the dynamics of the changes in C E A and Ca 19-9 levels. (Sheet 4). The positive ET U S G finding in post-operative phase in the correlation with the change in C E A and Ca 19-9 levels are treated as an absolute indication for the "second-look" operation. In the case of the unclear ET U S G finding we make a transperineal bio-psy under the sonographic control with the following histological examination of the taken material. (Sheet 5).
The comparison of the rectal carcinomas' invasivity determined by ET U S G in pre-operative phase with the invasivity determined by histological examination from operative preparate showed the consensus in 91,6 per cents. The recurrence of the malignant disease was found out by 23 patients from the set of 212 patients operated in the period of January 1st, 1987 to December 31st, 1997. (Picture 6,7). "Second look"



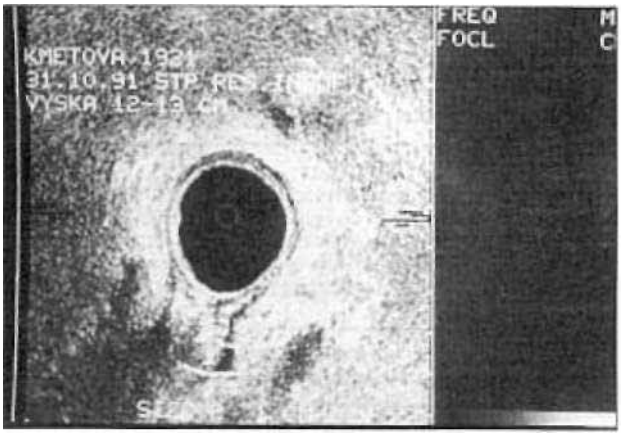
Picture 4: Rectal tumour in the stage uT.



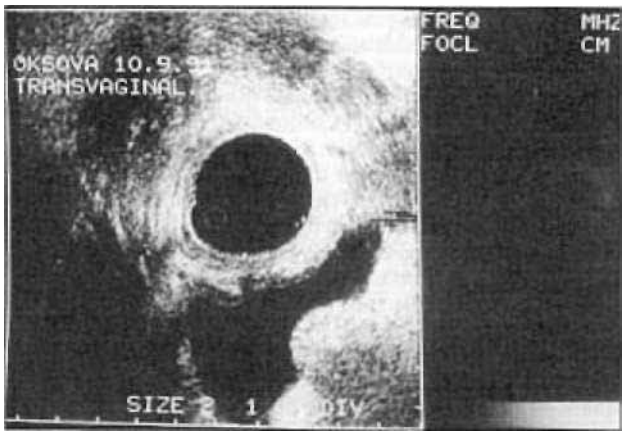
Picture 5: Rectal tumour in the stage uT



Picture 6: Recurrence of the rectal tumour



Picture 7: Recurrence of the rectal tumour



Picture 8: Transvaginal endosonography with endorectal sound probe - Recurrence of the Carcinoma canalis analis after the operation according to Miles

radical operations were made by 16 patients, e.g. 69,5 per cents. We made just palliative performances by 7 patients. By 16 radically operated patients we compare by ET U S G determined invasivity of the malignant process with the invasivity of the malignant process verified histo-pathologically. The correct invasivity of the malignant process was by ET U S G determined by 88,2 per cents of the patients.

Discussion

Application of ET U S G in the clinical practice meant the important extension of the diagnostics modality as well as of the low-sided rectal carcinomas' surgical therapy - by the selection of the operative modality. (1,5,7,11). Former used clinical criterions by digital examination according to Mason seem to be in comparison with ET U S G very imprecise. Experienced surgeon approached only 40 per cents of the ET U S G staging determining by the Mason's judgement. (5). There have occurred new possibilities for an early detection of the rectal carcinomas' local recurrences after sphincter saving operational performances in the post-operative period. We are able to verify the carcinoma's recurrence in the pelvic floor or in perineum already in its pre-clinical phase by women after the abdominoperineal amputation of the rectum. (Picture 8), (2,4,7,8). ET U S G has become a sovereign method of the examination by the determining of the rectal carcinomas' staging. The ET U S G sensitivity by the pre-operative determining of the rectal carcinomas" staging is proclaimed in the range of 90 up to 93 per cents. (1,10). The sensitivity in the post-operative period is up to 88 per cents. (1). ET U S G is irretrievable by the valuation of the relation, resp. distance from a tumour's low margin to a puborectal sling. There is possible to diagnostic also the primary rectal tumours or their recurrences (less than 2 cm) by ET U S G . CT or MR cannot do such diagnostics. The examination is not painful; manipulation with the probe is very easy. The interpretation of the obtained sonographic transversal cut of the rectum is obvious. In the case of any doubts mainly by the recurrences can the surgeon make his finding more objective by using the transperineal biopsy under the sonographic control. The endoprobe has the equipment that enables to make a targeted punction and acquire the biopsy from the examined place. The fact, that endosonic probe is rigid lays stress upon the experiences by using of the sound higher than 10cm from the anal margin. There is necessary to secure the rectal diameter of at least 2cm by the examination that can be treated as an disadvantage. In spite of the

endoprobe's high price is the examination economically advantageous because of minimal operational costs as well as physical wearing-out which can be proved by the fact that all examinations I had made with the same equipment from the beginning. (Sheet 6).

In accordance with the specialisation of our working place the importance of ET U S G by judging the integrity of the puborectal sling of the rectal sphincter apparatus has become higher in last time. I see the perspectives of the ET U S G also by the judgement of the periproctal inflammable affections and in the judgement of the gynaecological malignant diseases' invasivity.

Conclusion

In spite of the fact of no doubts about the ET U S G importance for pre-operative determining of the rectal carcinomas' staging and for the early diagnostics of their recurrences after the sphincter saving operations, there are only two devices in the whole Slovak Republic, these enables to make ET U S G with obtaining of transversal cut of the rectum in 360 degrees. The devices with the sector sound probe do not have the needed sensitivity of the examination, as well as there are many difficulties with the interpretation of the obtained sonographic picture. Herewith is necessary to realize that the surgeon and urologist can mutually use the device together with the endosonic probe. This fact has been already proved at our working place.

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THE CAUSES AND PREVENTION OF ANASTOMOTIC LEAK AFTER COLORECTAL SURGERY

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The cause of the leakage may be multifactorial, including contribution from faulty technique, ischemia of the intestine at the suture line, excessive tension across anastomosis and mesentery, the presence of local sepsis, presence of obstruction distal to the anastomosis. The old patient (>80 years), anaemic, malnourished with several coexisting diseases, receiving high doses steroids, after chemio-radiotherapy is more prone to develop the anastomotic leakage. The presence of any of these risk factors calls into question the safety of the planned anastomosis.

Anastomotic leakage is the most significant complication after colorectal surgery especially after anterior resection and it is the major cause of postoperative mortality and morbidity. Definition of clinically apparent anastomotic leakage is following: fistula to the skin or vagina, fever above 38°C or septicaemia in patients with radiological or endoscopic leak, with presence of intraperitoneal abscess or symptoms and signs of peritonitis in the presence of an anastomotic leakage [1]. (Fig. 1)

Its frequency is higher after anterior resection. In 60% of cases leakage heals under the conservative treatment. If re-laparotomy is necessary the mortality related to this complication is very high.

The leak incidence varies from 3.4% to 40% (the larger figures include subcUnical radiological diagnoses) [5]. In the series published after 1990 in the group of 1318 patients the rate of clinically detected anastomotic leak was 4.7%, varying between 2.7 and 10.5%. In an addition 5.7%-10.7% of patients had subclinical leaks discovered by routine postoperative radiological examination [2,3]. Goligher in 1970 found radiological leak in 69% of patients with low colorectal anastomosis diagnosed by means of routinely performed barium enema on 5-7-th day after surgery [4].

Our personal leak rate is 5.7% among 263 patients who underwent colorectal resection and primary anastomosis.

The consequences of anastomotic leak are peritonitis, fistula formation or abscess.

The principles of the good and reliable colorectal anastomosis are as follows: (Fig. 2)

1. good exposure and access to large bowel (long enough incision)
2. adequate blood supply of anastomosed stumps
3. prevent sepsis or gross faecal contamination
4. sutures or staplers should be properly placed assuring good approximation of all layers of bowel wall (most important is submucosa)
5. no tension of the anastomosis (always release the splenic flexure in left colorectal surgery)
6. prevent distal obstruction
7. the patient should be well nourished and large bowel should be mechanically well prepared (no faecal contamination) (Keighly1993)[17].'

Good exposure includes:'long incision, adequate bowel mobilisation, appropriate illumination, correct positioning of assistants and retractors.

Blood supply is essential for the healing of anastomosis. The cut ends of bowel should bleed. To assess the adequate blood supply of the bowel stump the routine measurement of tissue oxygen and laser Doppler flowmetry are currently being eva-

Fig.l

Definition of anastomotic leak

1. Faecal fistulas to the skin or vagina
2. Fever > 38 °C or septicaemia
3. Radiological or endoscopis signs of anastomotic leakage
4. Also an intraperitoneal abscess or peritonitis in the presence of an anastomotic leak

Müller, 1994

Fig. 2

The Principles Of Large Bowel Anastomosis

1. Good access and exposure
2. Adequate the blood supply of two ends of bowel (no clamps)
3. Sutures or staples should be properly and meticulously placed (layers appprocimation, the role of the submucosa)
4. No tension on the anastomosis (relase of the splenic flexure)
5. No faecal contamination (ideally empty the large bowel)
6. Prevent distal obstruction
7. The patient should be well nourished

luated in many centres. To achieve a good blood supply some important operative precautions should be followed, namely: adequate mobilisation, no tension on anastomosis, sutures must not be placed too deep or too tight (extramucosal sutures are the best in this aspect) used bowel clamps should be non-crushing and should be lightly applied without including the mesentery since that may compromise the blood supply.

Manual sutured anastomosis.

Since Czerny (1880) recommendation a two layer technique of colorectal anastomosis was commonly used. The first layer was an inner through-and-through suture which was either continuous or interrupted and the second layer (usually interrupted) was an outer serosomuscular Lambert stitch.

Halsted (1887) and Gambee (1951) showed that the submucosa was the strongest layer of the bowel wall and they supported the single layer technique with moderate inversion. Currently generally accepted view is that for colorectal anastomosis the inversion techniques should be employed.

Dunn and other authors stated that everted anastomosis should not be performed in patients with abdominal infections, after radiotherapy, with inflammatory bowel diseases [6]. These are risk factors for anastomotic leakage especially after stapling technique employed.

Kusunoki showed no significant differences in anastomotic dehiscence (5-7%) or recurrence of Crohn's disease between the stapling and hand-sewn procedures [7].

These results indicate that stapling technique producing an everted anastomosis is a safe procedure for Crohn's disease. Still exists controversy about the need for a one or two layer anastomosis. Theoretically the two layer anastomosis produces more ischemia, the tissue necrosis and more narrowing of the bowel lumen than one layer technique.

Currently for low colorectal extraperitoneal anastomosis one layer manual anastomosis is recommended. A two layer anastomosis is performed in more proximal colon whenever it is reasonable to do so. In many centres most surgeons opt to use the circular staplers.

To perform a two layer anastomosis the absorbable material is used for inner layer and non-absorbable material for an outer layer.

A single layer anastomosis is accomplished using a non-absorbable material usually monofilament, which causes less tissue reaction. New developed long-resorbable materials, like vicryl, PDS, maxon, are recommended for one layer colorectal anastomosis. The size or gauge of the suture material is usually 00 or 000 for adult intestinal anastomosis and the needle is of the round type.

There are numerous variations in technique to perform anastomosis. Most common are: end-to-end anastomosis (double layer, single layer full thickness, single layer extramucosal) end-to-side anastomosis, side-to-side anastomosis.

End-to-side anastomosis many surgeons prefer to perform following right hemicolectomy or after low rectal anterior resection. Most essential is to secure the mesenteric and antimesenteric corners by using the Connell stitches. Personally, I prefer to anastomose short distal rectal stump to side of proximal colon employing end-to-side technique (so called Baker technique).

An alternative to manual techniques is the use of staplers. Staplers have allowed colonic or rectal closure and anastomosis is performed more quickly than manually.

There are three types of stapling instrument which are applied in colorectal surgery. These are linear staplers (TA or RL), the linear cutters (GIA or PLC) and the circular instrument (EEA or lLS).

Whether stapled anastomosis is more tight and reliable than conventional hand-sewn is open to debate. Reported leak rates after stapled and hand-sewn anastomosis were 8% and 27% respectively.

Thirteen randomised, controlled trials showed a little or no differences between hand-sewn vs. stapled anastomoses in outcome variables including mortality, technical problems, leak rates, wound infections, strictures and cancer recurrences [8].

Strictures and intraoperative technical problems were more common with stapled than hand-sewn anastomosis. Thus both techniques are effective, stapled technique is a little bit quicker but the choice may be based on the personal preference.

Hashemi showed, that side-to-side stapled anastomosis is associated with lower incidence of recurrence in Crohn's disease requiring reoperation (2%) at 46 months with comparison to the end-to-end hand-sewn anastomosis (43%) [28].

However longer follow-up is required to evaluate this technique in randomised prospective study.

Docherty and co-workers in randomised, controlled trial evaluated 732 patients who had had any form of elective or emergency colorectal resection or reconstruction. In patients having suturing or stapling of anastomoses was equally effective. In patients who had colorectal anastomoses, incidence of radiological leak were lower when staplers were used [29].

Factors influencing anastomotic healing.

The morbidity and mortality related to anastomotic breakdown in colorectum is considerable. Fielding (1980) in his study showed, that among 1466 patients who underwent large bowel anastomosis there were 191 patients with an anastomotic leak with 22% of hospital mortality compared with 7.1% of 1275 patients without a leak [9].

Anastomotic leak can only be prevented if the causes are understood. Many factors may play a pathological causative role, including: (Fig. 3)

1. poor surgical technique
2. wrong intraoperative judgement
3. local complications (sepsis, bowel preparation, drains, role of omentum and peritoneum, anaesthetic drugs, protective stoma)
4. systemic complications (nutritional status, blood loss)
5. surgeon-related factors, which are of the most important causes of an anastomotic leakage.

Local sepsis

The presence of local sepsis (e.g. perforated diverticulitis, a perforated colorectal cancer, colorectal trauma, faecal contamination during colorectal surgery) causes the reduction in collagen at the colonic anastomosis. This may result in higher anastomotic dehiscence rate.

Fig. 3

Factors Affecting Anastomotic Healing

1. Poor surgical technique
2. Wrong or lack of intraoperative judgement
3. Local complications (sepsis, bowel preparation, drains, role of peritoneum and omentum, drugs used during anaesthesia)
4. Systemic factors (nutritionale state, bloods loss)
5. Surgeon-related factors, which are of the most important causes of an anastomotic leak

Fig. 4

The Principles Of Large Bowel Anastomosis

	(+)	(-)
anastomotic leak	8.1%	4%
wound infection	1.0.8%	7.4%

Plattel, Dis. C Red. 1998, 41, 875

Bowel preparation

Most surgeons use mechanical bowel preparation before colorectal surgery as essential in preventing complications. It is generally accepted that faecal loading has an adverse effect on the healing of large bowel anastomosis. A meta-analysis conducted by Platted showed that there is a limited evidence in literature to support the use of mechanical bowel preparation in patients undergoing colorectal surgery [10]. (Fig. 4) Three clinical trials showed a significant greater incidence of wound infection and anastomotic leak in patients who received a mechanical bowel preparation (10.8% and 8.1% respectively) comparing with patients without preparation (7.1% and 4% respectively) (fig 1). Remembering mentioned above there is a little doubt that is safer to leak from an empty bowel than from one that is loaded with faeces. (Fig. 5)

Recently again Miettinen and co-workers demonstrated, that preoperative bowel preparation seems to offer no benefit in elective open colorectal surgery in regard of mortality, wound infections and anastomotic leakage rate [11].

Protective stoma

Some surgeons advised to create a defunctioning stoma in order to prevent faecal contamination of an anastomosis and when anastomotic leak appears.

The decision whether to create a protective colostomy or ileostomy is often not a matter of objective reason but one of emotion like feeling that operation was technically difficult to perform, there was considerable blood loss, the tumour was stuck in the pelvis, the patient had many medical problems, the anastomosis looked tenuous, there was some tension across the anastomosis, I didn't feel good about it, I'll sleep better tonight. All those are reasons for protecting the anastomosis with a proximal stoma.

Probably the most common reason for a subsequent anastomotic complications is tension in suture line (distraction, vascular insufficiency). If the above precautions are taken a protective colostomy is usually unnecessary. There are relative indications for protecting the anastomosis which are following: pelvic sepsis, excessive blood loss and arterial hypotension, poor nutritional status and ultralow anastomosis (below 6 cm from the anal verge).

It is generally believed that a temporary defunctioning colostomy is avoided more often if a stapled anastomosis is performed than if a hand-sewn technique is used.

However recent experimental evidence in rats demonstrates, that a proximal diverting colostomy may reduce of collagen metabolism, anastomotic protein level and delay of the development of anastomotic strength [12,13,14].

There is no evidence that protective stoma prevents the anastomotic leak. On the other hand all surgeons know, that if leak does take a place in patient with diverting stoma, the septic complications resulting from the anastomotic dehiscence are significantly reduced.

Wessex (Grabham) colorectal audit showed, that a defunctioning colostomy reduced the frequency of anastomotic leak from 11.4% to 6.5% [15]. Reoperation was needed more frequently where there was no protective stoma (7.3% vs. 3.0%). Postoperative mortality was greater following a leak, where no diversion was performed (10.4% vs. 4.1%). (Fig. 6)

Presented data showed, that diverting colostomy decreases both the frequency and consequences of anastomotic leakage following anterior resection. More experienced surgeons use more frequently defunctioning colostomy performing low rectal anastomosis.

Tube caecostomy as a mean of protecting the low rectal anastomosis is advocated to facilitate postoperative management and to avoid the need for defunctioning stoma requiring formal closure having own morbidity and mortality [16].

However, intraluminar intracolonic bypass technique using coloshield or condom is a very safe, cost-effective and easily available alternative for coloanal anastomosis [19,20].

Hirsch et al. stated, that removing completely blood, serum, cellular debris from pelvis following resection of rectum and mesorectum minimises the risk of anastomotic breakdown. They believe that with this, routine defunctioning colostomy is no longer required for most patients undergoing low anterior resection with total mesorectal incision [26].

Drains which are situated in direct and close distance from anastomosis may contribute to anastomotic leakage and sepsis [17,18]. This must be considered when surgeon decides to drain abdominal cavity. Abdomino-perineal resection is the only colorectal procedure for routine drainage.

It is difficult to assess the role of peritoneum and of the omentum in prevention of anastomotic breakdown. There is no controlled trial in man, which support the technique of wrapping an anastomosis with omentum or peritoneum as the prevention of leak. However several surgeons do this manoeuvre whenever [17].

Fig. 5

Colorectal surgery

	wound infection	*death*
only mechanical preparation	36%	11.2%
mechanical preparation with antibiotic prophylaxis	22%	4.5%

Fig. 6

1996 - Wessex Colorectal Audit: Anastomotic Leak After LAR

	diverting colostomy	no diverting colostomy
frequency of the leak	6,5% (p=0.043)	11.4%
need of reoperation	3.0% (p=0.0024)	7.3%
postoperative mortality	4.1%(p<0.05)	10.00%
more experienced surgeon (> 10 operations/year)	leak<6.9%, proximal colostomy in 49.6%	
less experienced surgeon (<10 operations/year)	leak >14.1%, proximal colostomy in 30 %	

Fig. 7

Intraoperative Air Text To Asses
The Anastomotic Tihgtness

Test performed - in 23% of cases air leak, additional sutures, on 10th day after operation the radiological leak in 7.5% of cases, mortality 2%

Test not performed - on 10th day postoperatively the radiological leak in 23.5% with mortality 10%

Fig. **8**

Risk factors for development of an anastomotic leak (1726 pts)

1. LAR vs. other procedures (leak 4.4% vs. 1.4%, *p<0.001)*
2. Pre-existing sepsis vs. no-sepsis (5.0% vs. 1.*5%,p<0.005)*
3. Heavy intraoperative faecal contamination vs. minimal contamination (11.3% vs. *23%,p<0.001)*
4. Perianastomotic drains vs. no drain (6.3% vs. 1.9%, *p<0.001)*
5. Proximal diverting stoma vs. no stoma (9.8% vs. 1.*9%,p<0.001)*
6. Emergency vs. elective surgery (4.1% vs. 1.9%, *p - ns)*

We are concerned about the integrity of an anastomosis, about anastomotic blood supply, particularly in elderly patients and these with severe atherosclerosis or cardio-respiratory insufficiency. It is important from the practical point of view to assess the anastomotic integrity by using intraoperative air test (cycle tire puncture manoeuvre).

Once anastomosis is performed the pelvic cavity is filled with saline, intestinal clamp is applied proximal to the anastomosis and 50-100 ml of air is slowly and gently injected through the anus. No bubbles means anastomotic tightness. In case when bubbles appear an additional suture on the anastomotic line is required [12]. In the group of patients to whom intraoperative air test was performed in 23% of cases air leak was observed. This was an indication for additional stitches to secure anastomosis. On 10-th postoperative day the radiological leak in 7.5% of cases was showed and overall mortality in this group was 2%. In the contrast, in group of patients to whom intraoperative air test was not performed, postoperative radiological leak was found in 23.5% of cases with 10% mortality [12]. (Fig. 7)

Anaesthetic drugs

Neostigmine which reverses the effect of the curare-type relaxants might evoke active contraction of the intestine after completion of the anastomosis and subsequently might result in its disruption.

Current evidence suggests, that neostigmine should be avoided during colorectal surgery even with combination with atropine. Halothane anaesthesia, however, abolished this neostigmine adverse effect [17].

It is widely accepted that corticosteroids have a deleterious effect on healing of skin wounds. Little is known about effect of steroids on the healing of colonic anastomosis.

Schrock et al. (1973) found that administration of corticosteroids did not increase significantly incidence of clinical anastomosis leakage (retrospective study) [21].

From experimental study Furst et al. reported that steroids do have an adverse effect on colonic anastomotic healing [22]. It requires further clinical as well as experimental investigations.

Antineoplasmatic drugs can potentially adversely affect the healing process of large bowel anastomosis via several mechanisms like impairment of the synthesis and maturation of collagen, retardation of production and function of the cellular mediators of the healing process (macrophages, fibroblasts, leukocytes, epithelium). Hananel and Gordon in their experimental study demonstrated the 5-fluorouracil and leucovorin introduced in several regimens have no effect on the colonic anastomosis healing process [23]. Surgery, at least in experimental animals, can be performed safely during and shortly after chemotherapy.

Systemic factors

The role of systemic factors in aetiology of anastomotic leak is not yet completely defined. Among systemic factors at least three of them do seem to play a significant role and they are:

1. malnutrition (serum albumin level below 3.0 g/dl)
2. anaemia - Hb below 11g% and hematocrit below 33%
3. excessive blood loss and advanced malignancy.

Excessive blood loss results in reduction of colonic blood flow with subsequent tissue necrosis. Blood loss inevitably leads to the need of transfusion, which in turn has been shown to decrease the patientis immunocompetence.

Other risk factors

Averbach et co-workers published very interesting results of an analysis of risk factors for anastomotic leak after double-stapled low colorectal resection. The incidence of anastomotic leak was directly related to extent of proximal colon resection [24].

Standard colon resection for sigmoid colon-to-rectum anastomosis was associated with 1 % leak rate compared with 29% leak after transverse colon-to rectum anastomosis. Averbach presents also a risk factors list of anastomotic leak after low anterior resection [Table 1].

The most important factor for prevention of anastomosis breakdown is a good surgical technique that can improve with experience. The mobilisation of splenic flexure (with high ligation of the inferior mesenteric vein) is essential to decrease the tension across the anastomotic line and subsequently to prevent anastomotic dehiscence. In case of the narrow pelvis of small male patients or in patients with a bulky tumour a triple stapling technique (TST) is advocated in which a proximate linear stapler is used twice for transverse occlusion of the rectum. Staplers are fired from both sides of the rectum. The centre of the rectum with crossed staples is removed by a further procedure that is as the same as the standard double stapling technique [25].

Anterior resection for rectal cancer is associated with higher incidence of anastomotic leak. Total mesorectal excision (TME) reduced the incidence of local recurrence of the tumour but inc-

Fig. 9 Treatment of patients with anastomotic leak

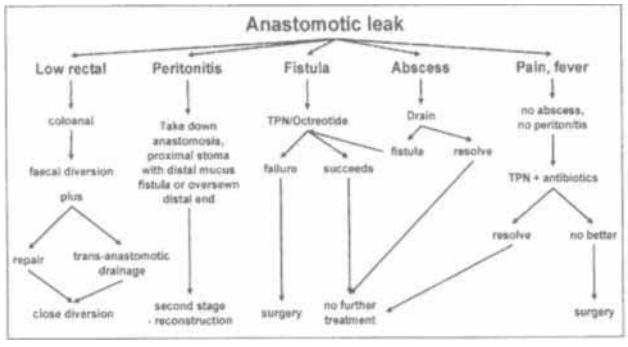


Fig. 10

LAR - functional outcome
median anastomotic height above anal verge -6 cm

	present	absent
„neorectal" volume at distention, pressure of 40 and 50 cm H_20	reduced	114 ml
compliance at sensation of filling	reduced	~ 4 ml/cm H_20
urge to defecate	reduced	~3.5 ml/cm H_20
maximum tolerated volume	reduced	~3ml/cm H_20

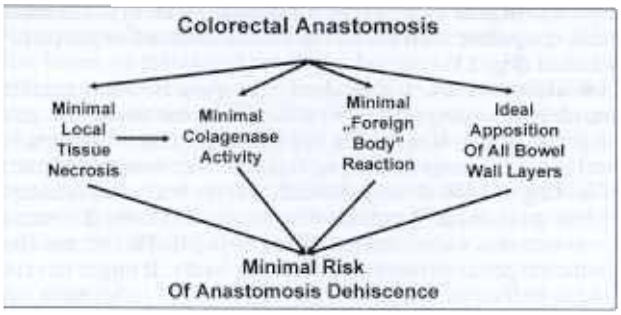
Fig. 11

Multifactorial Index Risk Factors in Colon Resection
(Ondrula et al., Dis. Col. Rect. 1992)

Risk factor	FunctionCoefficient	Clinical Index
Emergent	0.590	6
Age ≥ 75 years	0.420	4
CHF	0.363	4
Prior radiation	0.292	3
Albumin > 2.7 g/dl	0.227	2
Prior MI	0.206	2
COPD	0.142	1
Diabetes	0.121	1
Steroids	0.084	1

All risk factors have a significance level of p=0.031
CHF – congestive heart faluire; COPD – chronic obstructive pulmonary disease

Fig. 12



reased the rate of anastomotic dehiscence. Karanjia reported 11% of major anastomotic leaks associated with peritonitis and 6.4% of asymptomatic leaks detected by contrast enema.
All major leaks occurred at an anastomosis situated below 6 cm from anal verge. Defunctioning stoma reduces the incidence of major leak and protects against the development of peritonitis. It has been considered it prudent to defunction the low rectal anastomosis below 6 cm from anal verge, particularly after total mesorectal excision [27].
With meticulous attention to the technical issues described below anastomotic complications can be kept to less than 5% of the bowel resections.

Technique

a) Conventional suturing – suture ›, interrupted or continuous, should take deeper muscularis and minimal mucosa, good approximation all layers of bowel wall; the floor of the pelvis is not reconstituted but is vigorously irrigated with saline; no drains are advised
b) Stapled anastomosis – various stapling technique can permit a secure anastomosis. Following principles are essential for minimising complications related to the use of staplers:
   I. Use the largest calibre of stapler the anastomosis can accommodate
   II. After placing of the purse-string the excessive bulk of tissue should not appear around shaft
   III. The purse-string can be snagged up close to the shaft
   IV. Reinforce the purse-string if one is concerned about the possibility of a gap
   V. Repair any identified defect
   VI. Non-satisfactory anastomosis (e.g. incomplete doughnuts) mandates a diverting colostomy or evidence of primary anastomosis.

Most common factors leading to anastomotic leak are: disease of the bowel itself, inadequate blood supply and diseases that affect local blood flow particularly in distal stump, tension on the suture line, inaccurate suture placement, trauma and failure to obtain a watertight seal.
The implementation of intraoperative air testing or direct visualisation of anastomosis by means of the sigmoidoscope can reduce the leak rates from 14% ("no test" group) to 4% ("test" group).
The presence of drains is associated with an increased incidence of anastomotic leakage. Drains may adversely affect an anastomotic healing. Selectively used protective colostomy does not prevent the development of anastomotic leak but when it happens colostomy reduces the mortality and morbidity.
Low anterior resection, pre-existing sepsis (before operation), heavy faecal contamination during operation, perianastomotic drainage, proximal diverting stoma, emergency operation, cardio-respiratory insufficiency and less experienced surgeon: these are most essential risk factors for the incidence of an anastomotic leak. (Fig. 8)
The prompt diagnosis of anastomosis leak has a paramount value for the patient. Contrast enema with either uropolin or gastrographine enables early diagnosis of anastomotic leak.

Determination of lysozyme content in the wound or in the effluent from pelvic drains might be useful in early diagnosis of anastomotic dehiscence.
Lysozyme is a component of local defence and is produced in macrophages. In patients with impending anastomotic leak, lysozyme activity is significantly increased as early as the first postoperative day in contrast to patients without any anastomotic complications [30].
Total parental nutrition, broad spectrum antibiotics, treatment of the septic shock and prompt surgery (depends on patient status and diameter of fistula) are essential for the patient.
Disconnection of breakdown anastomosis followed by Hartman procedure is a treatment of the choice in anastomotic dehiscence bigger than 1 cm. (Fig. 9)
Long-term functional outcome after LAR may be impaired by anastomotic leakage [31]. In patients with leak as the results of pelvic sepsis, the fibrosis may develop with subsequent narrowing of the distal bowel or stricture formation. (Fig. 10)
"Neorectal" volume at distension pressures of 40 and 50 cm H2O and compliance at sensation of filling urgency maximum tolerated volume were significantly reduced in patients with anastomotic leak. The impaired anorectal function is measured by:
1. increased frequency of bowel movements
2. increased urgency
3. increased incontinence score and
4. impaired evacuation.

In addition anastomotic leak may increase the risk of locoregional neoplastic recurrence [32].

Summary

Several systemic and local factors play significant role in aetiology of anastomotic leak.

Systemic factors are: shock, sepsis, advanced age of patient (above 75 y.), coagulopathy, steroids, advanced malignant disease,

Table 1
Risk Factors of Anastomotic Leak after Low Anterior Resection of the Rectum (Surgical Treatment Only)

Demonstrated in randomised trials
Low (below peritonea reflexion) vs. high anastomosis
Implicated
Inadequate blood supply; tension on suture line
Septic conditions or undrained pelvic collection
Preoperative radiotherapy, chemotherapy, steroid therapy
Patients condition (concurrent disease), age
Inadequate bowel cleaning or emergency or palliative surgery
Shock during surgery, coagulopathy
Vitamin C, iron, zinc, methionine and cysteine deficiency (unbalanced collagen lysis/synthesis)
Implicated especially to double-stapled technique
Mucosal tears caused by anvil or staple gun insertion
Excessive upward traction of rectal stump during insertion or closing of an instrument
Forceful extraction of an instrument
Failure of staples closure

Adapted from A.M. Averbach et al. Dis. Colon Rectum 1996, 39, 780

radio- and chemo-therapy, diabetes, uraemia, anaemia, iron, zinc, cystein, vitamin C depletion, malnutrition with hypoalbuminemia, congestive heart failure and chronic obstructive pulmonary disease. (Fig. 11)

Local factors are: intraabdominal sepsis, bowel preparation, defunctioning stoma, peritoneum, omentum, drains, anaesthetic drugs. It seems to me that local factors and particularly surgeon-related variables are far more important. Fielding in 1980 clearly showed, that the leak rates amongst 84 surgeons in 23 hospitals who performed 1466 colorectal anastomoses varied from 0.5% to 30% [9]. This means that some surgeons perform anastomosis badly. It might be related to individual surgical technique, lack of judgement and low case-load.

Having some risk factors, which might impair the healing process of performed anastomosis I recommend the following procedures:

1. to avoid primary anastomosis and two-stages operation (Hartman or Hartman-like operation) should be performed
2. one-stage colorectal resection with primary anastomosis with anastomosis protection using intracolonic bypass tubes like biodegradable tubes, coloshield, condom (Wan-Hee, Ger, Ravo) [19,20].
3. Intraoperative air test for the assessment of tightness of the anastomosis
4. the proximal ileostomy or colostomy routinely performed in ultra-low coloanal or colorectal anastomosis particularly in patients presenting risk factors

Minimal local tissue necrosis, minimal collagenase activity, minimal "foreign body" reaction and ideal apposition of all layers of bowel wall of both anastomosed stumps (particularly submucosa) warrant that minimal risk of anastomotic dehiscence will take place. (Fig. 12)

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STERCORAL PERITONITIS

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Summary: Stercoral peritonitis (fecal peritonitis) as the gravest contamination of the abdominal cavity remains still very severe event followed by high morbidity and mortality rate. The most common origin of perforation is diverticular disease and colorectal tumor, other origins are accidental. The treatment consists of surgery and intensive medical care. Successfull can be only resectional surgery, when a septic source is taken away, contamination is stopped and a belly is cleared. The problem is a low ability of critically ill patient to undergo an operation. The usage of peritonitis severity and general condition classifications can help with decision about surgical procedure and can influence a treatment strategy.

The issue gives a review about some aspects of a stercoral peritonitis. AuthorĎs work-place experience based on the treatment of 13 patients with stercoral peritonitis during a period of 15 years is shortly presented.

Key words: Stercoral peritonitis - origin - classification - surgery - prognosis.

Stercoral peritonitis (fecal peritonitis) as the gravest contamination of the abdominal cavity remains still very severe event followed by high morbidity and mortality rate. J.C.Goligher wrote more than thirty years ago that "treatment of the carcinoma of the colon complicated by perforation and peritonitis make very melancholic reading", documenting this opinion by 90% mortality by patients with stercoral peritonitis from perforation of stercoral ulcer and 70 % mortality after perforation of growth (9).

The urgent laparotomy and surgical treatment of the site of perforation as well as cleaning of belly represent also nowadays the main surgical principle. The availibility of very intensive perioperative care and other medical progress involved this entity as well and improved the results. Stercoral peritonitis is a rare condition of various origin and different gravity, leaving several possibilities for surgeon decision depending on the conditions found to be present. That is the reason for making some review about causes, classification, surgical and general treatment and nowadays results.

The origin of large intestine perforation

Colonic carcinoma is one of common causes of stercoral peritonitis. There are two main sites of perforation: growth or proximal part of bowel, usually ascending colon, involved due to diastatic perforation from long-lasting complete distant obstruction. The frequency of perforations represents some 15 - 25% of all urgently operated on colonic tumors, only exceptionaly more than 30 % , in Czech literature the frequency ranged from 2 - 25 % incidency (Hájek, Maňhal, Vlasák, Vysloužil; summ. in 13) what represents usually the ammount from 10 to 30 patients. These datas agree with majority of articles presenting simmilar count of treated patients usually during ten years period (18,22,25), the major group is uncommon (5). The average patient age about seventy corresponds well with the top of incidency of colorectal cancer. Tumor stage III and IV predominates (18). The attention is concerned with tumor stage and resectability of the lesion but the description of the peritonitis degree peritonitis is usually hidden. The opinion that tumor patients with perforation are considered to have a bad prognosis and a reduced long-term survival will be discussed bellow.

According to the frequency **diverticular disease** is the most frequent cause of perforation and stercoral peritonitis. The ammounts of refered patients are major and reach a number of one hundred (6,12,22,28). Remarkable is the group of 300 patients with complicated diverticular disease in national British audit (31).

The peritonitis severity stratification using Hinchey score or MPI allow a comparison of treatment modalities and results and also to aproximate, that stercoral peritonitis represents one fifth of all peritonitis of diverticular origin.

Other diseases lead to colonic perforation with less frequency. Despite the fear of diastatic perforation in **colonic pseudoobstruction** only 1 report on Medline was found.

Hirschprung disease can also cause free perforation. Free colonic perforation in inflammatory bowel diseases especially in **ulcerative colitis** is a result of toxic megacolon. While Goligher stated the incidence 2 - 3 % at 60' (9), 20 years later Softley reported only 0.3 % (27). In patients with **Crohn's disease** the slow increase to 1.5% is registred, free perforation without toxic megacolon is more frequent than in UC (21).

Stercoral peritonitis can occur in some inheritary diseases, it means in **systemic diseases,** in patients with impaired collagen metabolism - **Ehlers-Danlos syndrom type IV,** or in endocrinopathies; perforative peritonitis associated with **parathyroid adenoma** were described (11). The perforation can occur without any known cause or concomitant disease as a **spontaneous perforation;** rare reports (30) and Medline document some 70 cases in recent literature. Despite to the denomination "spontaneous" some role of **ischemia** participates due to alterations of the intramural vascular pattern (3). Curious perforation due to colonic **scyballas** even in the end colostomy were reported (26).Finally **solitary colonic ulcer** as a origin of perforation was described (17). Colonic perforation can occur as a result of blunt or penetrating **abdominal injury,** as an complication of ingested **foreign bodies,** e.g. chicken bones, or introduced per anum. Iatrogennic origin includes colonic perforation as a complication of long-term medical therapy, e.g. **corticoids or NSAIDs** (14), as a serious complication of **transplant surgery** of kidneys and lung (23), or as a complication of abdominal vascular surgery. The large spectrum of perforations arises from **colonic endoscopy,** both diagnostic and therapeutic these events thanks to empty bowel and early recognition have got (fortunately) a good prognosis.

Location

The common site of perforation is a distant part of the colon, especialy **sigmoid colon.** It is the most common location of diverticular disease involvement and also of malignat growth. The perforation is possible at **all other parts** of large intestine, including appendix. The right colon is usually involved by diastatic perforation by colonic wall necrosis due to impaired blood perfusion through elongated and narrowed vessels. That is why it is recommended to check the transversal diameter of caecum by X-rays, the risk of perforation arises in diameter above 12-14 cm. Mentioned dilation should exclude the delay when surgery for distant colonic obstruction is indicated and supports the decision, when pseudoobstruction or bowel dilation by IBD is expected. Diverticular perforation can occur also on the right or transverse colon despite that fact, that diverticulas localised there are only few or even single. The most distal parts are perforated by introduced foreign bodies or spontaneously by hard stool.

Symptoms and diagnosis

No typical symptom exists for stercoral peritonitis. The **onset** ranged from sudden one
accompanied by peritoneal signs to sneaking distension of the belly with minimal other physical finding. The **patient history** should be taken into account namely in previous
palpable or US or CT detecable mass (1,31). The **general patient condition** range also from (rare) minimal alteration to grave septic shock. Pyrexia, grave tachycardia, leucocytosis and free air at **X-rays** intensifies expectation of the finding of generalized peritonitis with faeces in the peritoneal cavity (6,31).

Prognosis and classification of peritonitis

The prognosis depends on the severity of peritonitis, on the age, on general chronic and acute patient condition (including the advance of underlying malignant disease) and of the choice of a treatment.

Two classifications of peritonitis degree are commonly used - four stages **classification proposed by Hinchey** et al. **(22)** and the **Mannheim Peritonitis Index** - MPI - introduced by Wacha et al (20). While the first one describes only the extent of intraabdominal sepsis, the second one takes into account the age, gender, present organ failure, presence of malignity, duration and origin of peritonitis and finally the features of intraperitoneal content. In both Schemas stercoral peritonitis takes the gravest degree. According to these Schemas the recent datas about mortality of stercoral peritonitis range from 19 to 48 % (12,22,25,31).

The general statement changes are expressed by different scooring systems - the **APACHE,** resp. **APACHE II(16), SAPS** and **SAPS II (19), POSSUM (24)** and **HDWS** (8) are the most common.

While the **septic complications** have been responsible for the **immediate result** of surgical treatment, in tumor patients both an **advanced tumor** and septic complications of peritonitis have been made responsible for the **bad prognosis of malignant perforation.** Nespoli found worse prognosis for patients with tumor than diverticular perforation, probably related to more advanced age and to higher severity score of peritonits in patients with cancer (22). Some suggest an independent prognostic effect of perforation on survival and report significant differences in long-term survival after adjustment for tumor stages (25), the others demon

strate a significant influence of degree of peritonitis without the difference in long-term survival comparison between groups of patients with perforated to uncomplicated tumor. Patients with perforated tumors have got increased occurence of septic multiple-organ failure in comparison with benign perforations (18).

Surgery and general treatment

The treatment of peritonitis includes surgery and intensive medical treatment or resucsitation respectively. Both parts underwent significant progress and influenced a results.

The task of surgery is to localise a septic source, to stop a contamination and to clear up a belly. Safety considerations have led surgeons to perform as minimal procedures as possible in the past, respecting that the majority of patients was already very ill, compromised by shock and despite resuscitative measures never fit for an operation.

The minimal access using a stoma creation and drainage in acute surgery, initial stage of three stage procedure in resectional lesions, did not meet two first intentions sufficientely and resulted to the mortality about 50 % in the past and nowadyas as well. Acute resection as effective procedure removing the source of sepsis (even of malignancy) was adopted slowly from 50'. It improved surgical results and decreased mortality after colonic perforation to the level of 30 %. Another question occured: if to finish the surgery by stoma as the Hartmann's or Mikulicz's two stage procedure, or to perform the immediate anastomosis. Despite the interest of surgeons to convince that one of these methods is superior, studies failed namely in patients with complicated colorectal tumor. The survival benefit of single-stage ("primary") procedure was not summarily proven enough(25). Due to experience of high anastomotic laekages rate and persistent peritonitis and sepsis in patients with stercoral peritonitis a discontinuity operation remains the standard one for left-sided perforations untill nowadays (2,6,13,18). An extensive resection finished by ileocolic anastomosis represents an alternative method, which minimizes the risk of leakage to 5 %.

The analysis of results of methods used for treatment of colonic perforations is not free of problem. Nespoli et al. gave the results of treatment of stercoral peritonitis as follows: 20% mortality after primary resection and anastomosis, 40% mortality after Hartmann's procedure a 72% after simple colostomy (22). Simmilarly Kriwanek et al. presented 35%, 38% a 100% for patients with perforated tumors and 9%, 13% and 66% respectively for patients with benign perforations in the same sequale of surgical procedures (18). These results suggest that the mortality rate is significantly lower by primary resection rather than by Hartmann's procedure or by colostomy, but the choice of operation depends on the general condition; primary resections were performed with minimally alterated patients and the most simple procedures with desperately ill ones. So the real determinant of outcome is not the surgical procedure but the overwhelming septic process measured by scoring systems.

The segmental resection with ileocolic anastomosis is considered to be the optimal surgical option for treatment of stercoral peritonitis from right-sided lesions and the Hartmann's procedure for left-sided perforations (2,6,18,22). The extensive resection (subtotal colectomy) is recommendable for diastatic or multiple perforations.

The others procedures like suture of perforated site stand out of standard procedures.

Surprisingly in the literature a little attention is given to the maneuvers at the finish of surgery, e.g. to the **peritoneal lavage, drainage, stagged laparotomy or laparostomy**. The decision depends on the severity and duration of sepsis, and on the viability of visceras. In principle, only the drainage is appropriate already when no doubt about removing of all involved tissue and complete clearing out of the belly (29). The stagged (scheduled) re-laparotomy allows to check the abdomen and remove fluid collections unavailable other way. Laparostomy enables to decrease intraabdominal pressure.

The **intensive medical treatment** on **ICU** is needed beginning at the admission for treatment. Central venous and urinary catheters, electrolyte and volum replacement and resuscitation of circulation instability are the priorities of the whole perioperative period, including the artificial ventilation in some patients. Broad-spectrum antibiotic therapy is obligatory. It is necessary to remind that no preparation can improve the condition in patient with stercoral peritonitis basically and that the surgery should not be postponed (4).

Respiratory, urinary and wound infections are the most common postoperative complications. The postoperative morbidity and mortality are caused usually by a cardiac decompensation or by multiple organ dysfunction (2,6,22,25).

Own experience

During the period of 15 years 87 patients with peritonitis of large intestine were operated on. There were 38 males (average age 76.4 years) and 49 females (average age 71.3 years). According to the origin the tumor caused the peritonitis in 46 cases, in 39 of them due to perforation of the tumor, by 7 patient due to distant perforation. Diverticular disease caused the peritonitis by 32 patients, ulcerative colitis by 3 ones. 7 patients were operated for peritonitis of other origin. From the whole group of patients stercoral peritonitis was registred by 13 patients. The origin was tumor by four, diverticular disease by five; ulcerative colitis, pancreatitis, blunt abdominal injury and ischemia was simmilarly the origin every by one patient. There were performed two segmental resections, one stoma and one subtotal colectomy by tumor perforations, two last quoted died; myocardial infarction and multiple organ failure were the causes of a death. Three tumor lesions were resectable, one was advanced and fixed. The spectrum of operations for perforations of diverticular origin consists of one stoma creation with drainage, one Mikulicz procedure and three segmental resections; two of them were finished with a anastomosis and one as a Hartmann's procedure. The last surgery was finished as laparostomy. The patients after stoma surgery and after Mikulicz procedure died, both from organ failure. The patient with perforation by ulcerative colitis underwent subtotal colectomy and survived. All three patients operated on for perforations of different origin underwent segmental resections, two of them survived, one of them had got a laparostomy. In the whole group 11 colonic resections were performed and 2 stoma surgeries with drainage, two cases were treated by laparostomy. Five deaths were registred (38.5 %).

Discussion and conlusions

Despite simmilar finding of faecal content in the peritoneal cavity the entity of stercoral peritonitis differs according to origin, duration, septic involment, general condition and age. The peritoneal signs are usualy a reason for surgery, supported only by some patients by X-rays, CT and US finding. Already present or comming manifestation of septic shock is obvious and requires an intensive care. Without any doubt an intensive care management contributes to success of treatment significantly , but even an adequate care is not effective enough before the surgery and removing of the intraabdominal sepsis (2).

The surgical treatment is hopefull only when radical surgery eliminates the septic contamination with sure (6,12,22,25) The extensive surgery is limmited mainly by patient condition; a choice of operation type should take into a count the value of some scoring system. While one stage procedure with bowel continuity restoration even by stercoral peritonitis leads nowadays to same immediate results as an discontinuity procedure (22,25), the majority of surgeons (including author) prefer a discontinuity ones (13).

It is possible to conclude: stercoral peritonitis is an extreme condition even for experienced surgeon. It requires a fast recognition, well intensive care, radical surgery to be effective enough, as well as beeing performed gently enough not

to put down the patient. Even already 2400 years ago it was Hippocrates who noted typical signs predicting an early outcome - pointed nose, halo eyes and cold ear auricles (10). Hippocrates is also an author of an aphorism saying that hopeless events need risky treatment. In connection with stercoral peritonitis both proclamations remains valid.

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PROGNOSTIC FACTORS IN RECTAL CANCER

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Identifying prognostic factors in rectal cancer is very valuable for choosing the method of treatment. Prognostic factors play an important role in making decision of margin of surgery, treating with pre- or postoperative radiochemotherapy. In last few years, apart from traditional clinical and histopathological factors, also genetic, biochemical and immunological factors there are taken in the consideration of the prognosis. In this study there has been used research records and publications from different clinical hospitals according to actual international literature.

Prognostic factors in rectal cancer might be divided into a few group:

1. Patient factors
2. Tumor factors
3. Concomitant tumor factors
4. Genetic and immunological factors
5. Factors associated with the treatment

The main **patient factors** which are actually taken as prognostic are:

- age
- gender
- family history of colorectal cancer
- general condition

Due to the aging of the general population, there has been a relative increase of elderly patients with rectal cancer. Prognosis depending on age is different for local recurrence rate and metastases from prognosis for 5-year survival. Metastases and local recurrence occurs less frequently in the elderly. Local recurrence rates decrease with age and it is respectively: 23% for age 15-64,18% for age 65-74,14% for age 75 and over. Different studies reported conflicting results of relationship between age and survival rate. 5-year survival seems to be similar in the three age groups, or a little better in the younger group. However, more favourable prognosis in younger patients is also connected with better general condition and it lowers the postoperative mortality rate, which is 1 % for patients younger than 60 years, than it steadily increases with age and for patients 80 years and older the operative risk is 10%. On the other hand, the youngest group with colorectal cancer includes patients with hereditary tumors, in which the risk of local recurrence and secondary tumors might reach even 80%. The 5-year survival in this group is only 41% for patients younger than 60 years, compared with 70% for patients with a negative family history.

Gender is thought to be the most independent patient predictor of recurrence and tumor-related mortality. Male patients have a worse prognosis compared with female patients. In stage I rec-

tal cancer, male patients have a recurrence rate of 15%, which is greater than the 5% recurrence rate of females. The 5-year survival of male patients in this stage is only 85% compared 98% survival rate for female patients. There was some speculations that outcome differences between male and female patients might be related to the extend of lateral clearance, because wide lateral margins are more difficult to obtain in the male pelvis. However, differences have been still present between male and female patients group with similar lateral and distant resection margin and similar numbers of recovered lymph nodes. More recently male gender has been shown to be an independent adverse prognostic factor also in patients with stages II and **in** rectal cancer.
A general condition is rather subjective factor. Mainly state of nutrition, anemia, coexisting diseases and liver function are considered. The liver function tests are thought as the most objective and significant of these factors. The abnormal liver function tests correlate with a short survival after surgery (examinated groups included patients with liver metastases).

The **tumor prognostic factors** are:
- **T** stage;
- Dukes' stage;
- tumor location;
- tumor mobility;
- size and depth of invasion;
- type of exenteration;
- presence of tumor ulceration;
- intratumoral blood vessel invasion (BVI);
- intratumoral lymphatic vessel invasion;
- neural invasion;
- histologic differentiation.

T stage and Dukes' stage remain basic factors in making decision of treatment. The table 1 shows correlation of T N M stage of colorectal cancer with Dukes' classification.

	T N M stage	Dukes' stage
Tis NO MO T1 NO MO T2 NO MO	I	A
T3 NO MO T4 NO MO Every T N.x MO	II Not staged	B
Everv T N1 MO Every T N2-3 MO	**III**	C
EveryT, every N, M1	IV	D

Nx - regional lymph nodes cannot be assesed

T N M stage is the strongest predictor of clinical outcome and it is confirmed as a factor with the strongest independent effect on survival. Survival rate is respectively: 77-84% for stage I, 56.1% for stage II, 34.8% for stage III, 0.0% for stage IV and 57% for not staged tumors. Approximately 25% of rectal cancer patients present with stage I disease. The rate of local recurrence in these patients is 7% for Tl and 12% for T2, but it increases even to 48%, when other risk factors like male gender; blood vessel invasion and poor differentiation coexist. Adjuvant chemotherapy plus pelvic radiation has evolved as a standard of care for rectal cancer patients with stage II or III disease. It is not recommended for stage I rectal cancer, except the group of high-risk patients in which adjuvant therapy reduced the rate of recurrence and lead to an improved survival.
Tumor location is valuable prognostic factors in primary rectal cancer. Patients with proximal rectal cancers (>6 cm from the anal verge) have lower recurrence rate and better survival prognosis than patients with tumors of the distal rectum (< 6 cm from anal verge). Some authors suggest that an anterior tumor location has a significantly higher survival rate than other positions. Two-thirds of anterior tumors are of pathologically favorable Dukes' stages. However, the majority of studies provide that the posterior-located tumors, as infiltrating mesorectum instead of other organs, give better possibility of total excision. So that, in patients with posterior-located tumors the risk of recurrence is lower, and prognosis of survival is better.
Tumor mobility remains a dominant prognostic factor in patient selection and choice of surgery.
Size of the tumor is defined by its largest diameter more or less than 40 mm. This factor is significant in stage I disease only. Survival rate is 50.1% for 40 mm or less and 43% for more than 40-mm tumor diameter.
Rectal tumors with the infiltrating type of growth have a significantly worse prognosis than those with the expanding type. Expanding tumors have a well-delineated and circumscribed border of growth, while infiltrating tumors have cluster or single cells leaving the tumor mass and spreading into the bowel wall. Infiltrating tumors present more often blood vessel invasion and have much higher risk of recurrence and metastases. Better survival rate in patients with the expanding tumors (63.6% compared with 25.1% in infiltrating tumors) might be connected with the earlier diagnosis because of bleeding from rectum, which is a symptom often associated with these tumors.
The recurrence rate is a little higher in patients with tumor ulceration (15% compared with 10% for non ulcer tumors). Survival is similar for both tumor types.
Patients with either intratumoral vascular or lymph vessel invasion have a worse survival prognosis. Blood vessel invasion (BVI) is an independent predictor of recurrence and tumor related mortality in stage I disease. Male patients with BVI have a rapid rate of recurrence with almost 100% recurring by 24 months. Survival rate in all patients at stage I with BVI is 66%, compared with 80% in patients without BVI. In male patients with BVI mortality is 80% by 36 months. In patients with more advanced rectal cancer vascular or lymph vessel invasion is associated with an increased incidence of hepatic metastasis.
Pattern of tumor differentiation is usually described using two main features: glandular configuration at the histological level and nuclear polarity at the epithelial cell level. Tumors are described as well, moderately and poor differentiated. In poorly differentiated and undifferentiated tumors, glandular configuration and nuclear polarity are almost completely lost. Survival rate is strictly correlated with tumor differentiation and it is 72% for well, 47.5% for moderately and 25.4% for poorly differentiation tumors. Another histological factors of prognostic value are lymphocytic infiltration and extent of fibrosis. Survival rate is significantly higher in patients with extensive lymphocytic infiltration and little fibrosis in tumor. D N A ploidy and S-phase fraction can be measured easily on an intraluminal biopsy specimen before therapy is instituted. S-phase fraction (the percentage of cells in the S phase) determines the tumor proliferative activity. S-phase fraction is a statistically significant predictor of survival, especially in Dukesi C patients. Patients with S-phase fraction 10% or greater have 17 time greater chance of dying of rectal cancer, than patients with S-phase fraction less than 10%. On the other hand, tumors with a low S-phase fraction exhibit a higher local recurrence rate. This has been postulated to result from the relative resistance to radiotherapy of slowly proliferating cells.

The main **concomitant tumor factors,** which influence prognosis are:
- extrabowel skipped cancer infiltration
- lymph nodes metastasis
- liver metastasis
- synchronous primary or secondary tumors

During a pathologic examination, cancer nodules, and not lymph node metastases are often seen in the fatty tissue outside the rectum. This type of cancer spread is called extrabowel skipped cancer infiltration (ex) and indicates the aggressive biologic activity of rectal cancer. The overall recurrence rates after curative surgery are 58% for ex(+) group compared with 24.0% for ex(-) group. The ex(+) group exhibited a significantly worse survival. Therefore an extended dissection, postoperative adjuvant therapy seems to be necessary for patients with ex.
Lymph nodes metastases correlated with a short survival. Presence of lymph node metastases is included in T N M classification. Recent studies indicate that an accurate search for metastases in lymph nodes smaller than 5 mm in diameter seems to be important for staging. Researches demonstrated metastatic involvement in 50-78% lymph nodes measuring less than 5 mm in diameter. The use of monoclonal antibodies against cytokeratin in detecting occult microembolic metastases in lymph nodes of Dukes' stage B patients may improve the accuracy of pathologic staging. Presence of cytokeratin positive cells in the lymph nodes correlated with a poorer prognosis and it is indication for aggressive adjuvant therapy.
Liver metastasis is a poor prognostic factor. The mean survival time is 8.5 months for all patients. Prognosis is even worse in case of bilateral hepatic involvement, multiple tumors, abnormal liver function tests and other distant metastases.
In case of synchronous secondary tumors prognosis is very poor. Synchronous primary tumors might indicate hereditary character of disease.

New treatment strategies need to be coordinated with evolving knowledge about **genetic and immunological factors** connected with rectal cancer. There are:
- c-Ki-ras mutations
- C-myc mutations
- A P C gene mutations
- expression of C D44 variants 6 and 8-10
- nuclear p53 overexpression
- DCC-protein expression
- preoperative carcinoembryonic antigen level

c-Ki-ras and C-myc mutations have been implicated in tumor initiation and progression. A P C gene, p53 and D C C are also tumor suppressor genes implicated in rectal tumor carcinogenesis.
The relation between phenotypic expression in patients with familial adenomatous polyposis (FAP) and the site of mutations in the A P C (adenomatous polyposis coli) gene was examined. Germline mutations in the A P C gene cause FAP. Patients with severe polyposis have an increased rectal cancer risk. Present data support an association between severe polyposis phenotype and mutations at A P C gene codons 1309 and 1328. For other mutations phenotype is more variable. The prognosis in patients with these mutations is poor. Rectal cancer in these patients has a predisposition for local recurrence. Total proctocolectomy with end ileostomy should be performed in case of colorectal cancer in these patients.
C D44 variants 6 and 8-10 have been known as the useful marker of tumor progression. About 50% rectal tumors are positive for C D44 v.6 and v.8-10. There is significant correlation between CD44 immunoreactivity and both lymph node and hematogenous metastases and high recurrence rate. Survival rate is significantly lower in C D44 v.6 and v.8-10 positive cancer. Therefore C D44 v.6 and v.8-10 may be a biological prognostic markers.
Nuclear p53 protein is closely related to the development of postoperative recurrences of rectal cancer and has higher predictive value than standard pathological variables. Positive overexpression is more frequent in tumors with blood vessel invasion, p-53 - positive tumors show a higher likelihood of relapse and lower survival. The tumor-suppressor gene p53 encodes a transcription factor that plays a critical role in the induction of G1 cell cycle arrest and apoptosis after D N A damage. The rate of apoptosis is strictly correlated with the therapeutic effect of hypertermochemoradiotherapy. This effect occurs through apoptosis. This combined therapy can induce an additive or synergistic anti-tumor effect in rectal cancers with wild-type p53 as well as in those with mutated p53 through papooses, offering new therapeutic opportunities and a better prognosis.
D C C protein, for which a gene is located on chromosome 18q has recently been reported to have a prognostic value in colorectal cancer in predicting metachronous distant metastases after treatment. Expression of D C C protein was assessed in tissues from patients who developed distant metastases but no local recurrence. Nonexpression of D C C protein has an negative influence on survival for all tumor stages. In stage **II** cancers the negative predictive value was 88%. So, D C C is a useful prognostic marker in patients with rectal carcinomas for survival and occurrence of metachronous metastases.
High preoperative carcinoembryonic antigen level correlated with local recurrences, distant metastases and low survival rate

In prognosis of rectal cancer also **factors associated with treatment** are considered, such as:
- the number of lymph nodes found in resected specimens
- circumferential margin involvement
- postoperative septic complications
- adjuvant pre- and postoperative therapy

In patients without involved lymph nodes the long-term survival and local recurrence rates are significantly better when more than 10 lymph nodes are present in resected specimens. When fewer than 10 nodes are found, whatever the cause, adjuvant radiotherapy has to be considered, especially in patients having infiltrating T3 tumors.
Circumferential margin involvement is more an indicator of advance disease than inadequate local surgery. Both disease-free survival and mortality are related to margin involvement. Recurrent disease has been seen in 50% of the patients with a positive margin.
The actual survival rate of patients with major septic complications (like anastomotic dehiscence, peritoneal abscess) is significantly lower than that in noncomplicated cases. No statisical difference is observed in the survival of patients with minor septic complications (wall abscess).
Adjuvant pre- or postoperative chemoradiotherapy improve survival in **II** and **III** stage disease and in high-risk patients at I stage.

Conclusion
In patient selection and choice of treatment many prognostic factors should be considered simultaneously. Both recurrence rate and survival rate depend on many factors connected with each other. With the Cox model the following prognostic index (PI) was formulated:
PI = 1.37 x (gender)... 2.05 x (age)... 0.06 x (tumor status) + 1.85 x (type of exenteration)
-1.46 x (treatment)... 2.91 x (chemotherapy) + 2.83 x (S-phase fraction)
1.34 x (D N A ploidy)
When the parameter values are:
gender: 0 for male; 1 for female
age: 0 for <54 years; 1 for >54 years
tumor status: 0 for primary; 1 for recurrent
type of exenteration: 0 for posterior; 1 for anterior or total
treatment: 0 for other; 1 for irradiation and surgery:
chemotherapy: 0 for other; 1 for chemotherapy and surgery and radiation
S-phase: 0 for 9%; 1 for 10% or more
D N A ploidy: 0 for diploid; 1 for aneuploid.
According to PI, low-risk patients (PI of less than 1.37) have a 5-year survival rate of 68%, whereas high-risk patients (PI of 1.37 or more) have a survival rate of 24% only.

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PROGNOSTIC FACTORS IN RECTAL CANCER

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Nearly 50% of patients operated for rectal cancer die of recurrent or metastatic disease, despite approximately 75% of them have undergone resection with curative intent. The difficulty to know the real prognosis of the disease has stimulated many studies aiming to establish some factors influencing its outcome. Three are the components to consider in the prognosis of a patient with a rectal cancer: the tumor, the host and the surgeon.

THE TUMOR

An unquestionable prognostic factor is the stage of the tumor at the moment of the diagnosis and treatment. A careful clinical and instrumental preoperative evaluation permits a precise macroscopical staging of the disease and, in most cases, a consequent proper approach. Digital examination, transanal ultrasound, pelvic CT permit a good preoperative evaluation while other investigations (colonoscopy, abdominal U S, M R) can exclude syncronous cancers or metastatic spread (1,2).
Dukes' classification with its variants and T N M are generally accepted and numberless are the studies about their prognostic validity. A careful histological evaluation of the tumor is the essential step to know the stage of the disease and to evaluate the utility of an adjuvant treatment.
Regarding the micrometastasis in the lymph nodes in rectal cancers Dukes A and B, a recent study has demonstrated that they cannot be considered as a prognostic marker and their presence don't imply different strategies for additional theraphy or follow-up (3).
Many authors have published studies about factors considered as expression of biological malignancy of the disease.
Tumor D N A content has been described as having a prognostic significance in patients with colorectal cancers. It's unclear whether tumor ploidy as a prognostic factor is indipendent of various standard prognostic variables such as depth of invasion and lymph nodes involvement by the tumor. Nevertheless some studies seem to demonstrate that the marker plays an important role in indicating a biologic aggressiveness of the disease (4,5).
P53 expression has demonstrate no prognostic value for overall survival or local control in a recent accurate study (6), while the Urokinase type plasminogen activator (uPA) seems to be a promising prognostic factor in Dukes B and C rectal cancers (7). Same results has been achieved using the Thymidylate Synthase (TS): patients with colorectal cancer and TS positive tumor seem to have a poorer prognosis(8).

THE HOST

The immunologic response of the patient with rectal cancer doesn't seem to have a direct influence on (he outcome of the disease. Hypoalbuminemia, loss of weight, need for blood transfusions, concomitant systemic diseases certainly can have a negative influence on the outcome of the disease but the results of many studies about these factors don't permit to consider any of them as an indipendent variable in the prognosis of patients with rectal cancer.

THE SURGEON

Local recurrences after resection for rectal cancer can vary between 0 and 21%. Also if some of these variations can depend on selection of patients it is likely that the surgical

technique is the most important variable. Many technical factors are involved in the resection of a rectal cancer and can play an important role in the outcome of the disease.
1-High or low ligation of the inferior mesenteric artery: there are no prospective controlled study on this subject but seems that a high tie is not necessary and can increase the risk of nerve injury.(9)
2- Total mesorectum excision (TEM) Studies on the local spread of rectal cancer have demonstrated that continuous or discontinuous extensions of the tumor involve the mesorectum and that its excision with envelope of fascia intact can highly reduce the incidence of local recurrence. (10,11,12)
This finding has led the concept that a T E M must be an indispensabile step in the surgery for rectal cancer. Spread of the tumor distally within the mesorectum rarely exceeds 2 cm and it's probably unnecessary to remove the whole mesorectum for tumors of the upper third of the rectum. If the tumor is found by the pathologist at the circumferential resection margin, this can be considered as a factor of poor prognosis in terms of distant metastasis and survivals 13)
3- Extended lymphadenectomy: The Japanese are the main proponents of this technique that provides the removal of the lateral and superior lymphatic systems. This means the high ligation of the inferior mesenteric artery and an extended periaortic and pelvic lymph node dissection from the duodenum to the periaortic and lateral iliac lymph nodes. The main disadvantage of the technique is the increase of morbidity, particularly regarding the pelvic nerve injuries.(i4)
Up to date we don't know if the technique is likely to result in an improvement in survival.(15)

4- Irrigation of the rectal stump: Although we know that many neoplastic cells are shed into the lumen during a rectal excision, their viability has been a contentious subject. Recent data confirm this possibility: even so this mechanism of local recurrence is thought to be quite rare. It's therefore a good idea to irrigate the rectal stump with a cancercidal agent prior performing the anastomosis.
5- Resections of contiguous structures: A tumor that involves other structures has a worse prognosis than a tumor that's confined to the rectum. Nevertheless some studies have reported encouraging results after extended procedures. (16,17)
Probably the best results in these cases depend on a careful selection of patients. It's unknown if a less aggressive surgery combined with pelvic radiotherapy can achieve similar results.

In a recent prospective study 10 prognostic factors were correlated with recurrence and tumor-related mortality:
Patient factors: age, gender, preoperative C E A;
Tumor factors: location from the anal verge, stage, intratumoral blood vessel invasion (BVI), intratumoral lymphatic vessel invasion, tumor ulceration, histologic differentiation;
Surgical treatment: extent of surgical resection.
Indipendent predictors of recurrence were male gender and B V I. Indipendent predictors of tumor-related mortality were male gender, B V I and poorly differentiated tumors.(18)

Up to date the outcome of a patient with rectal cancer is the result of the host response in addition to the macroscopic and histologic findings of the tumor related to the volume of mesorectum excised by a good surgeon.

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THE USE OF ENVIRONMENTAL SCANNING ELECTRON MICROSCOPY (Aquasem) IN COLOPROCTOLOGY

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Summary: Aquasem is the environmental scanning electron microscope (ESEM) - a device which permits the direct observation, manipulation and analysis of many materials in their natural and unaltered state. The microscope operates under low vacuum and fresh or unfixed biological specimens are maintained wet in a separate chamber filled with water vapour. The aim of this study was to examine the mucosa of small and large bowel and anal canal.

Different sample preparation methods were used in 34 speciemen and the results were compared with the use of both conventional scanning electron microscopy (SEM) and E S E M. In the future, we are to examine the tumor surfaces of colon, rectum and anus.

Key words: environmental scanning electron microscopy, coloproctology, mucosa

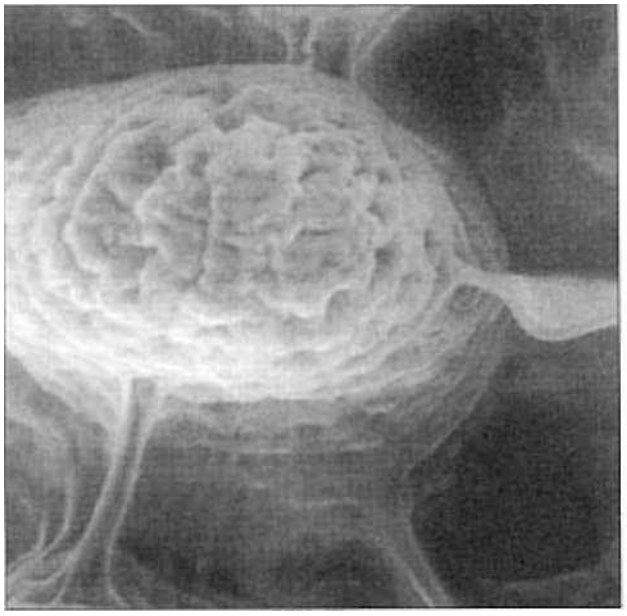


Fig.1
Ileal mucosa (x 520)

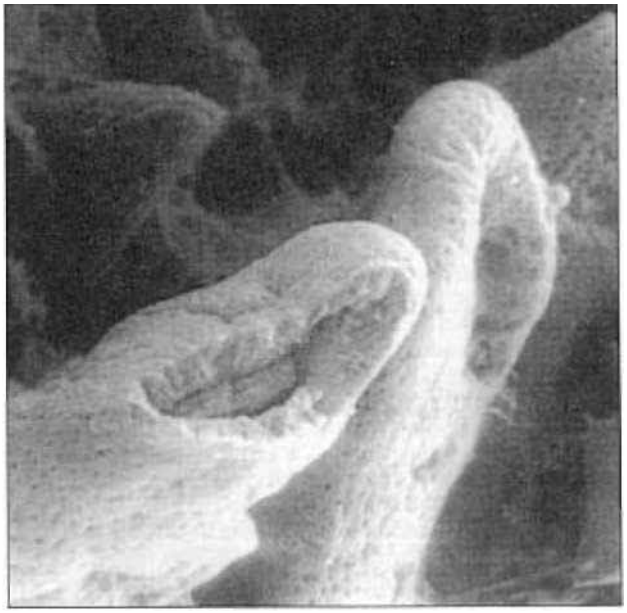


Fig. 2
Recta mucosa (x 370)

INTRODUCTION

In 1997 it was 100 years since the British physicist Thomson discovered one of the fundamental matterparticles - the electron. This discovery stimulated research activities in this field so much that, in a relatively short period, both electron mass and charge were determined and, using the laws of mechanics and optics, its movement was described. The finding that an electron beam of a defined energy behaved similarly to a light beam became the foundation for the construction of electron optical devices. In 1931 Ruska and Knoll put together the first transmission electron microscope and in 1939 its manufacture commenced. In 1938 Von Ardenne published his discovery of the scanning principle and when, in 1942, Zworikin used a scintillation counter for detection of secondary electrons, the first scanning electron microscope (SEM) in the world appeared *(Mráz and Polónyi,* 1988).

Initially, it was believed that, because of extreme conditions to which specimens are subjected, electron microscopy (EM) would not be a technique suitable for processing biological materials. In thel940s, preparation methods to separate specimens with high water content from the destructive effects of vacuum were still being sought. These trials, however, were not successful.

The development of S E M made remarkable progress with the advent of television. The S E M resolution power improved and the contruction of suitable detectors permitted the use of the great amount of information which comes from the interaction between electron beams and the specimen.

In spite of the fact that methods for preparation of biological specimens, including soft tissues and individual cells, have shown great advancement, their demands in terms of costs and time revived the idea of constructing a device which would allow the viewing of specimens in their natural state, i.e., with their water content *(Danilatos,* 1981).

The first attempts at this, conducted in the 1970s, were influenced by efforts to wrap the specimen in a thin film transparent to primary electron beams. This approach made it possible to produce electron micrographs of biological specimens at atmospheric pres-

Fig. 3
Meckel divericulum (x 300)

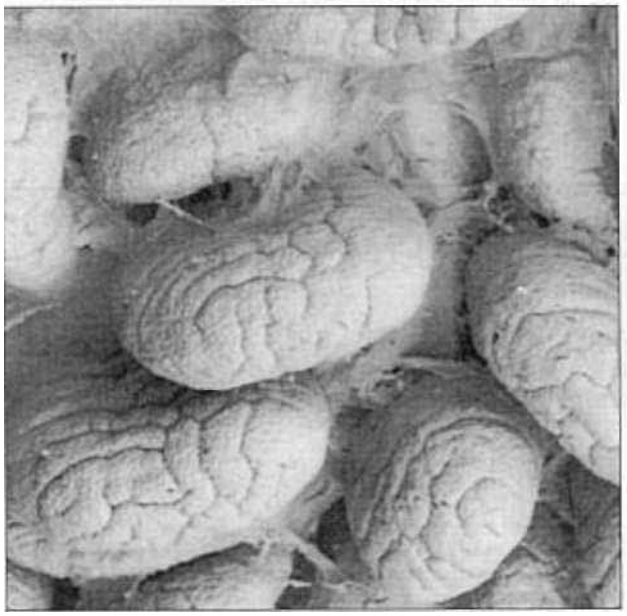
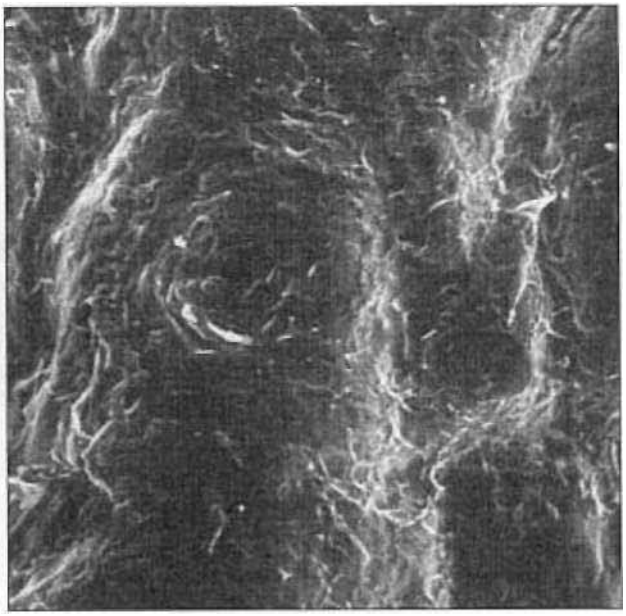


Fig.4
Unfixed wet specimen anal mucosa (x 370)



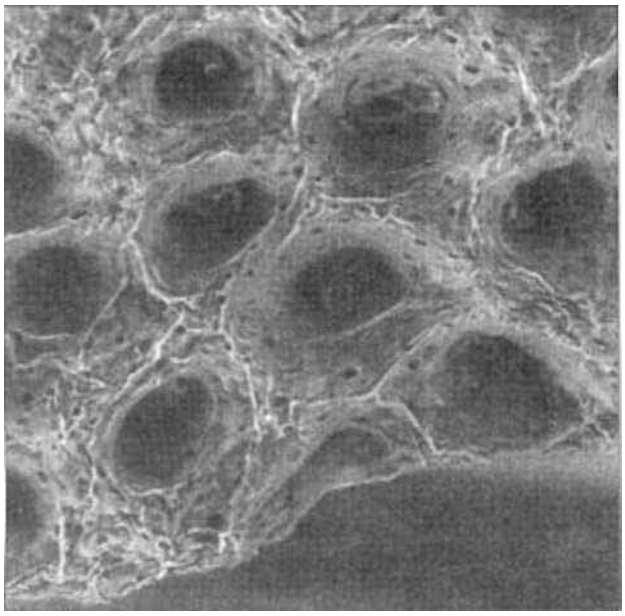


Fig. 5
Unfixed sample immediately after being placed in the microscope rectal mucosa (x 260)

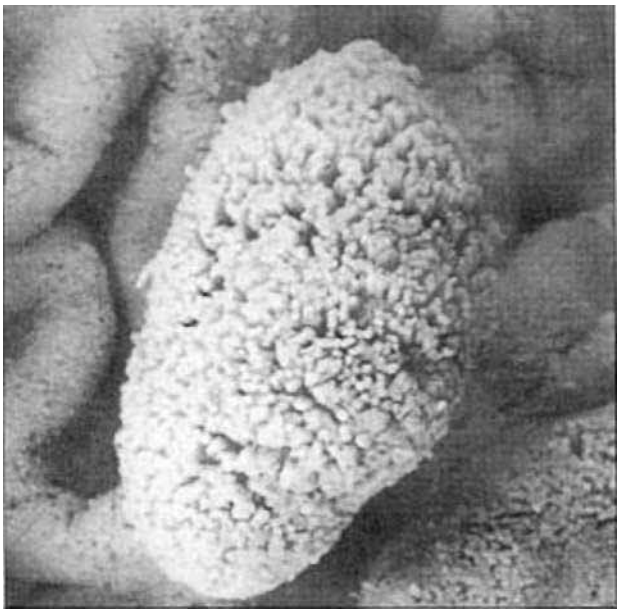


Fig. 6
PEG fixation rectal polyp (x 420)

sure *(Danilatos,* 1980). Useful results, however, were obtained only within the scanning mode, i.e., using transmission electrons *(Dupouy* et al., 1962; *Lane,* 1970).

Another approach was the construction of a specimen holder which permitted continuous diffusion of water vapour into the vacuum and production of a higher pressure zone around the specimen which is thus protected against deformation. Further improvement in this principle resulted in the construction of two-chamber vacuum systems. The high vacuum electron optics column is separated from the specimen chamber in which vacuum is regulated by a diaphragm with a minute aperture. These SEMs, termed High Pressure or, more often, Low Vacuum Scanning Electron Microscopes (LVSEM), do not facilitate direct insertion of specimens but have the advantage of allowing observation of non-conducting materials without metal shadowing *(Danilatos and Robinson,* 1979; *Danilatos,* 1991; *Shah and Durkin,* 1992).

The most accurate method for direct viewing of wet specimens has so far been achieved by separating the high vacuum chamber from the regulated vacuum chamber with the use of a differential pumping system. This principle has been developed, both theoretically and in practice, by the Australian scientists Robinson and Danilatos in the 1980s *(reference).* They introduced the designation Aenvironmentald' to emphasise that the viewed specimen is situated in a surrounding which is close to its natural environment. At the beginning of commercial use, some manufacturers tried to construct adapters to conventional electron microscopes. The first producer of environmental scanning electron microscopes (ESEM) was the PHILIPS Company which had bought the patent coverage from the American ELECTROSCAN Co. and, in 1995, introduced the SENXL 30 ESEM on the market.

In the same year the TESCAN Company in Brno presented an environmental scanning electron microscope under the name AQUASEM. This was the result of joint research and development activities carried out by a team of workers from the Institute of Scientific Instruments of the Academy of Sciences of the Czech Republic and from the Department of Electrotechnology, Faculty of Electrical Engineering and Computer Science, Technical University in Brno, supervised by Professor Autrata *(Autrata* et al., 1997). Their ESEM was based on a TESLA BS 434-PERLA electron microscope and some their own patents. The manufacturer of these microscopes became PRECIOSA CRYTUR, Ltd., Turnov.

This paper reports on our initial experiences with the AQUEASEM.

MATERIALS AND METHODS

Environmental scanning electron microscopy facilitates the observation of specimen surfaces without any special treatment, thus allowing time consuming processes of fixation, dehydration, drying and metal shadowing to be eliminated.

In this study, biopsy samples of human digestive tract tissue were used.These were collected, together with tissues for histological examination, from patients being operated on at the Department of Surgery, Masaryk Memorial Cancer Institute, Brno. The samples were fixed with 5% formaldehyde to preserve them during the period between surgery and observation.

The other samples included in this investigation were selected organs from insects, worms and mice.

After the relevant processing, the samples were viewed

1. Tesla BS 300 scanning electron microscope (after fixation, drying] and metal shadowing)
2. AQUASEM scanning electron microscope
   a) unfixed and wet
   b) fixed and wet
   c) fixed, dried and without metal shadowing
   d) fixed, dried and metal shadowed
   e) fixed twice and wet
   f) fixed twice, dried and without metal shadowing
   g) immersed in polyethylene glycol (PEG)

RESULTS AND DISCUSSION

In August 1997, an AQUASEM scanning electron microscope, which is a property of the Masaryk Memorial Cancer Institute, Brno, was installed in the electron microscope laboratory of the Department of Histology and Embryology, Faculty of Medicine, Masaryk University in Brno.

This computer-controlled ESEM facilitates the viewing of the surfaces of conductive, non-conductive and wet specimens, recording and saving enlarged images in the standard format onto computer recording media and further computer processing of the image.

This ESEM operates on the basis of a three-step vacuum system in which the differential pumping chamber is controlled by ahigh-speed rotary air pump and, together with a regulatory valve, maintains the appropriate gas pressure in the specimen chamber. The maximum pressure level set by the manufacturer is 1500 Pa. The differential chamber is separated by a diaphragm from the electronic optics and by a special crystal (YAG) from the specimen chamber.

The Y A G single crystal has been developed by the Institute of Scientific Instruments in Brno and has a mutiple function as an aperture diaphragm for the differential chamber, a scintillating detector and a gaseous secondary electron detector *(Autrata et al,* 1997a). The latteris function is to detect the gas (water vapour) ionisation in the vicinity of the specimen, which results in a significant amplification of the number of electrons detected and also suppression of positive charge accumulation on the specimen surface.

The A Q U A S E M operates with a directly-heated tungsten cathode at an accelerating voltage of 10 to 20 kV. In our observations involving soft, wet tissues, the resolution claimed by the manufacturer to be 10 nm was actually lower, due to the penetration of high energy primary electron beams deeper under the tissue surface. This outcome can partly be avoided by treating the material to be viewed with a fixation agent containing heavy metals *(Procházka and Ilkovics,* 1998; *Horký and Skřička,* 1998).

The computer accessories include a software programme (WinTip) for image analysis; some of its applications can be seen in Fig. 2. Using the high quality printer, an image comparable with a conventional electron micrograph is immediately available.

Our experience showed that the pressure of 700Pa used at room temperature was not sufficient to maintain the saturated vapour environment and this resulted in considerable deformation of soft tissue surfaces during specimen observation. Some of these conditions have also been mentioned by *Robinson* (1978) and *Gilpin* (1997). It is expected that this disadvantage will be solved by installing a water vapour developer and the Peltier cooling stage, thus allowing the stage temperature to be regulated. A reduction in temperature and vapour access should improve environmental conditions for viewing soft, wet tissues.

In order to verify that the results of specimen imaging with the use of the A Q U A S E M were fully comparable with those obtained with the BS 300 R E M , different wet specimens were observed. Wet solid materials, such as bone or gallstones, presented no problem when viewed in the A Q U A S E M . The preparation procedure could be reduced to a mere rinsing of the surface, followed by fitting the specimen into the holder. Neither deformation nor charging of the surfaces occurred. Similarly, specimens which included chitin or keratin as their major component, did not require any special preparation. It appears that the majority of data so far published in the E S E M field deal with solid samples *(Uwins et al,* 1993; *Gilbert and Doberty,* 1993; *Kaufman et al,* 1992; *Kodaka et al,* 1991; *Neubauer and Jenning,* 1996).

Tissues with a greater content of firm connective tissue and a semi-fine surface epithelium were also easy to view. They are subject to deformation only after a prolonged exposure to vacuum *(Horký and Skřička,* 1998).

Some problems appeared when samples of wet soft tissue were observed. After the specimen was placed in the vacuum, rapid evaporation of water occurred in spite of the fact that, in the specimen chamber, the pressure was maintained above 600 Pa. At the beginning when the surface relief was still covered by water, the ionisation detector did not mediate any image. After the surface water had evaporated, the relief became apparent but quickly became deformed, particularly if fine surface structures were present (Figs 1,2,3,4). The period between the evaporation of surface water and the subsequent deformation of surface structures lasted only a few minutes. Therefore, only a very short time was left for selecting a site to be viewed, adjusting the selected section at the desired magnification and final focusing. If tissue surface deformation occurs during exposure , the photograph will be out of focus *(Fujimaki et al,* 1990). Moreover, the situation is complicated by the use of a small viewing field at a large initial magnification (x300). It has been shown that, in such specimens, the magnification cannot exceed x 500 *(Procházka and Ilkovics,* 1998). In our observations, the disappearance of fine surface structures resulted in the fact that, at higher magnifications, the image no longer corresponded to the real state. (Fig. 5)

An attempt was made to delay surface deformation by subjecting the specimen to double fixation. While a single, though prolonged, fixation did not produce results different from those obtained in untreated tissues, the double fixation brought some improvement. In addition to an increase in contrast, the surfaces showed better resistance to deformation. This allowed the viewing of wet soft tissues routinely at a magnification of x 1000, and occasionally at x3000, with good resolution *(Procházka and Ilkovics,* 1998; *Horký and Skřička,* 1998). Further approaches involved the immersion of specimens in different media. P E G proved to be the best agent because it blends with both ethyl alcohol and water. After immersion it was possible to remove excess P E G from the tissue surface. When this procedure was combined with the double fixation, it was possible to achieve a good contrast with the differentiation of details at a high magnification and a reduced surface deformation. (Fig. 6)

We are planning to use the A Q U A S E M for specifying the categories of biological materials suitable to be viewed in their natural state as well as for targeted investigation of surfaces in various implants. The parameters are improved after installation of the Peltier cooling stage.

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