

Influence of neoadjuvant radio(chemo)therapy  
on wound healing in lower-rectal cancer  
patients subjected to abdominosacral resection  
(ASR)

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# Influence of neoadjuvant radio(chemo)therapy on wound healing in lower-rectal cancer patients subjected to abdominosacral resection (ASR)

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## Abstract

**Background:** Our previous experiences suggest a marked improvement of therapeutic results if abdominoperineal resection (APR) is substituted with abdominosacral resection (ASR) in lower-rectal cancer patients. Literature, however, indicates that the impaired wound healing might be associated with the implementation of neoadjuvant radio(chemo)therapy in cases subjected to APR or operated on using a sacral approach. Hence the aim of the study was to assess the frequency of wound healing complications in the clinical records of ASR-operated patients and to check whether it depends on the implementation of preoperative radio(chemo)therapy.

**Methods:** The analysis included 188 ASR patients, who were divided into three categories depending on the neoadjuvant treatment given: 1) long-term radiochemotherapy (RChT, n=34); 2) short-term radiotherapy (RT, n=20); and 3) no neoadjuvant treatment (n=134). Surgical wound healing was monitored during the initial four weeks (acute complications) or within one year (late complications) after the operation. Moreover, the duration of post-surgical hospitalization was monitored in each patient.

**Results:** Total frequency of wound healing complications was significantly higher in the RChT patients compared to other groups (47% vs. 15% in RT and 14% in no neoadjuvant groups). There were more cases of superficial (9% vs. 5% and 2%, respectively) and deep (29% vs. 10% in both the remaining groups) wound infections in RChT patients. The duration of postoperative hospitalization was not affected by the type of treatment, whereas it was prolonged by some healing complications.

**Conclusions:** Improper wound healing is infrequent in ASR-operated patients, unless this procedure was preceded by long-term RChT.

**KEYWORDS:** lower-rectal cancer, abdominosacral resection, ASR, rectal cancer, rectum, wound healing

**ABSTRACT:**

**Background:** Our previous experiences suggest a marked improvement of therapeutic results if abdominoperineal resection (APR) is substituted with abdominosacral resection (ASR) in lower-rectal cancer patients. Literature, however, indicates that the impaired wound healing might be associated with the implementation of neoadjuvant radio(chemo)therapy in cases subjected to APR or operated on using a sacral approach. Hence the aim of the study was to assess the frequency of wound healing complications in the clinical records of ASR-operated patients and to check whether it depends on the implementation of preoperative radio(chemo)therapy.

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**BACKGROUND:**

The implementation of total mesorectal excision (TME) resulted in a marked improvement of the prognosis in rectal cancer patients.<sup>1-3</sup> Therapeutic results vary, however, depending on the part of the rectum where the tumor is localized. Anterior resection (AR) is a safe procedure that is routinely performed in cases of malignancies located in the upper and middle third of the rectum. Its implementation, with TME principles, resulted in a marked decrease of local recurrences and an improvement of survivals.

A significant problem of modern oncological surgery, however, is related to cancers located in the lower third of the rectum. Routinely performed abdominoperineal resection of the rectum (APR), although done in accordance with TME guidelines, does not bring the expected results. This unsatisfactory outcome seems to be mostly related to the limited approach to the surgical field and the resulting high rate of circumferential margin (CRM) involvement. Consequently, local recurrence is frequently noted in lower-rectal cancer patients operated on by means of APR, and their survivals are significantly worse compared to upper- and mid-rectal cancer cases.<sup>4</sup>

Our experiences in the surgery of lower-rectal cancers suggest a marked improvement of therapeutic results if APR is substituted with the abdominosacral resection of the rectum (ASR).<sup>5</sup> The latter technique, known for more than a century,<sup>6,7</sup> offers new possibilities after undergoing a few technical modifications and when performed in accordance with TME guidelines. The wide surgical approach obtained due to coccygectomy (and – infrequently – also partial sacrectomy, S5 or S4+S5) allows for the performance, with direct vision, of a sharp excision of the entire rectum together with the ischiorectal space. These principle advantages of modern ASR result in

a lower frequency of specimen tearing and consequently in a decreased number of local recurrences similar to those noted in upper- and mid-rectal cancer patients.<sup>5</sup>

Since the publication of the German Rectal Cancer trial<sup>8</sup>, neoadjuvant chemoradiation has been routinely recommended for patients with locally advanced (stage II-III) rectal cancers. At least several studies, however, performed in low-rectal cancer patients who underwent APR preceded by neoadjuvant RT or RChT revealed adverse effects of such an attitude.<sup>9-11</sup> Also sparse reports on the application of the sacral approach in rectal cancer treatment suggest that related improper wound healing might be a limitation of the technique described, especially when combined with neoadjuvant RT.<sup>12-15</sup>

Our own modification of ASR completed by TME rules has been routinely performed in lower-rectal cancer patients at our Center since 1998. Consequently, we decided to assess the frequency of wound healing complications in the clinical records of patients who were operated on by that technique and to check whether it depends on the implementation of preoperative radio(chemo)therapy.

#### **PATIENTS AND METHODS:**

**Rectal cancer patients:** The retrospective study included 188 lower-rectal T2-T4 cancer cases (i.e. located up to 6 cm from the anal verge, median 2 cm, range 0-6 cm) qualified for surgery and operated on at the Regional Comprehensive Cancer Center in Wroclaw between April 15<sup>th</sup>, 1998 and March 31<sup>st</sup>, 2007. All subjects were operated on by the same surgical team using the standardized TME and our own-modified ASR-technique.

**Surgical technique of ASR:** Abdominosacral resection of the rectum done in accordance with TME standards was performed on all 188 patients. After the initial abdominal stage of the operation (TME technique) and colostomy formation, the rectal stump together with the tumor and swab located in the bottom of the pelvis on the level of the coccyx was left in the minor pelvis, and the abdominal cavity was closed in multiple layers. The anus was stitched in prone jackknife position. Subsequently, the skin was incised around the anus and the cut was elongated towards the sacral bone. The insertions of glutei muscles were cut from the last two sacral vertebrae. The coccygeal bone was separated with the aid of a gouge and removed together with S5 or S5+S4, whenever necessary. Subsequently, the presacral (Waldeyer's) fascia and the parietal lamina of the pelvic fascia were cut. The rectal stump together with the tumor and surrounding mesorectum were removed via the resulting wide opening. Subsequently, the anal levators were cut with the simultaneous ligation of the surrounding vessels. The rectum was cut off from the prostate or vagina under direct vision without excessive tension or manipulation that could result in specimen tearing. In cases of adherence or invasion of the primary tumor to surrounding organs, their *en bloc* resection was performed whenever feasible. A wide surgical approach and a gentle sharp resection that was performed under direct vision prevented inadvertent entry into the wrong plane. The perineal wound was closed without tension in multiple layers with a drain placed in the pelvis for two-three days.

**Wound healing analysis:** The analysis included all 188 patients (118 males and 70 women, median age 67 years, range 35-88 years) who were operated on by means of ASR. Patients were divided into three categories depending on the preoperative treatment they were given (Table 1):

- 1) 34 (18.1%) patients with T3 and T4 tumors (independently from N parameter) who received neoadjuvant treatment including external beam radiotherapy and chemotherapy (RChT, 50 Gy,

25 fractions, 5-fluorouracil + leucovorin) and underwent surgery six weeks after their last irradiation; 2) 20 (10.6%) subjects with T3 and T4 mobilized tumors (independently from N parameter) who received short-term radiotherapy (RT, 5 x 5 Gy) followed by an immediate operation (within two days after their last RT); and 3) 134 (71.3%) T2-T4 cases without any neoadjuvant treatment. Such an unequal distribution of neoadjuvant treatment methods was related to the fact that some patients from the RChT and RT groups participated in the randomized trial of the Polish Colorectal Group<sup>16</sup> and before 1999 preoperative treatment was not obligatory for T3-T4 cases. Healing of the surgical wound in ASR-operated patients was monitored and verified based on medical records during the initial four weeks (acute complications) or within one year (late complications) after the operation. Acute complications were defined as: 1) superficial infections (involving skin only), 2) deep infections (penetrating into the subcutaneous tissue), 3) abscesses, 4) dehiscence with subsequent granulation, and 5) dehiscence requiring surgical intervention, whereas perineal hernias found on physical examination up to one year post surgery were classified as late complications. Moreover, the duration of post-surgical hospitalization was monitored in each patient as an indirect measure of wound healing.

### **STATISTICS:**

The frequencies of certain wound healing complications were compared with the Fisher's exact test, whereas the durations of post-surgical hospitalization – with the Mann-Whitney U test. Calculations were performed using Statistica 5, Version 97 (StatSoft<sup>®</sup>, Poland) software, and statistical significance was defined as  $p \leq 0.05$ .

### **RESULTS:**

The frequencies of impaired wound healing reported in ASR patients from different groups and the median times of their postoperative hospitalization are summarized in Table 2. No postoperative mortality or eventeration were recorded in any of the patients studied. Total frequency of wound healing complications was significantly higher in RChT patients compared to other groups (47% for RChT vs. 15% and 14% for RT and cases without preoperative treatment, respectively). Moreover, there were more cases of superficial and deep infections in patients who received preoperative RChT. The only two cases of perineal hernia, however, were recorded in cases deficient with neoadjuvant treatment, but neither was symptomatic nor required surgical intervention. Nevertheless, the duration of postoperative hospitalization was not affected by the type of adjuvant treatment, although it was markedly longer in cases where there were some types of healing complications (Table 3). Deep infections, abscesses and partial skin dehiscence with granulation or necessitating surgical intervention significantly prolonged hospitalization. Acute wound healing complications in ASR-treated cases were observed in 38 of 188 patients and prolonged their median hospitalization by two days (12 vs. 10) compared to the cases without any healing problems. Antibigram-based antibiotic treatment and antiseptic dressings were used in such cases and usually provided proper healing of the surgical wound. Only ten cases (5.3%) of local recurrences were noted in the groups studied. The cumulative local recurrence rate was markedly higher in Dukes C cases compared to other stages. No cases of local recurrence were noted among patients who received short-term RT preoperatively, but this phenomenon seems to be related rather to the small size of that cohort than to any particular effectiveness of that form of neoadjuvant treatment. The local recurrence rate in patients subjected to long-term RChT preoperatively did not differ significantly compared to cases without any neoadjuvant therapy (Table 4).

Local recurrences occurred in 3 of 38 cases (7.9%) and in 7 of 150 cases (4.7%) with improper and proper wound healing, respectively. The number of local recurrence cases, however, was too small for any conclusions regarding the prognostic role of improper wound healing.

## **DISCUSSION:**

Our previous experiences suggest that due to the implementation of ASR the therapeutic results achieved in lower-rectal cancer patients will be similar to cases of mid- and upper- rectal cancer treated by means of anterior resection.<sup>5</sup>

An easy approach to the distal rectum and surrounding tissues seems to be crucial for the therapeutic success of the technique described. Consequently there is the possibility of total, under-direct-vision removal of all structures which might play a critical role in the development of local recurrences: the coccygeorectal ligament, anal levators and constrictors, and tissues of the infra-levator compartment.

Such a free approach is provided by a total removal of the coccygeal bone and – whenever necessary – by the partial resection of the sacrum. Previous reports on a similar approach in rectal cancer treatment, however, suggest that related improper wound healing might be a limitation of the technique described, especially when combined with neoadjuvant RT.<sup>12-15</sup> In all cases, however, coccygectomy+sacrectomy was carried out as part of the surgical treatment of recurrent rectal cancers, and its character was in fact palliative. No major complications in wound healing were in turn observed in our patients in whom ASR was the primary treatment for lower-rectal cancers, even in cases when the surgical procedures were preceded by short-term RT. Lack of complications in the latter group may have resulted from the fact that ASR was performed shortly

(1-2 days) after the last RT session. Consequently the surgical wound had healed before radiation recall developed. That hypothesis was proved by the results obtained in patients who received neoadjuvant RChT. The frequencies of wound healing complications and their severity were markedly higher compared to other groups. Even in the neoadjuvant RChT group, however, improper wound healing neither prolonged postoperative hospitalization nor required special surgical intervention including the VAC system application.

The combined application of APR and neoadjuvant radio(chemo)therapy in turn was shown to be related to the impaired healing of surgical wounds at least by several studies. In their analysis of 160 APR patients, Bullard et al. found that preoperative radiation therapy doubles the rate of total and major perineal wound complications.<sup>9</sup> Chadwick et al. proved that patients who have an APR (n=94) are over 10 times more likely to have perineal wound complications if they have preoperative RT rather than not.<sup>10</sup> Impaired healing of the perineal wound if RT or RChT is used to treat malignancies prior to surgery was also shown by Artioukh et al. in a cohort of 37 consecutive patients who underwent APR.<sup>11</sup> Christian et al., however, were the only ones who – similar to our results – revealed that preoperative radiation was not associated with increased complications following APR performed for rectal cancers in 153 patients.<sup>17</sup> Nevertheless, our previous experiences with the ASR technique suggested that optimal resection of the primary tumor, with no malignant cell deposits left in the surgical field, is crucial for successful therapy, regardless of its being combined or not (Bebenek, unpublished data).

We do not have an opportunity for direct comparison between the wounds related to ASR and APR, since the latter procedure is not in use at our clinic. Nevertheless, the confrontation between the topographical analysis of the region subjected to APR and our experiences with the

ASR technique indicates that the quality of the wound, following a properly conducted ASR, does not differ from the lesion related to APR. The posterior stage of the APR dissection is carried out with the patient in the lithotomy position. An elliptical incision is made around the anus. Wide margins are maintained while dissecting the rectum to the ischial tuberosity laterally, and to the tip of the coccyx posteriorly. Once this has been accomplished, the abdominal and perineal dissections are joined and the levator muscles are separated under traction to the lateral margins of the prostate glands or vagina. The specimen is passed to the posterior dissector and the rectum is removed, including any prostatic or vaginal margins. Compared to ASR the only difference in wound structure refers to the larger extent of the ASR-related lesion, resulting from the removal of the coccyx and S4-S5, if necessary. Well vascularized musculocutaneous tissues, however, enable the resulting wound to close properly and without excessive tension. Consequently, there is no need to create any kind of flap and/or fat approximation in the midline during the pelvic floor reconstruction.

An analysis of our relatively rich clinical material has revealed that improper wound healing is infrequent in ASR-operated patients and does not constitute a limitation for the application of ASR, especially in patients who have not received neoadjuvant chemoradiation. Optimal healing of the surgical wound in ASR-operated cases results mostly from an unlimited surgical approach with sharp and under direct vision dissection along anatomical planes. Moreover, both literature evidence and our experiences suggest that most rectal malignancies could probably have been cured by properly performed surgery alone, which is better than the traditional blind approach combined with radio- and chemotherapy, which in turn increases the risk of improper wound healing. Consequently, modern ASR performed in accordance with TME standards gives new, attractive perspectives for the surgical treatment of lower-rectal cancers.

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**TABLE 1****Characteristics of pretreatment in ASR patients subjected to wound healing analysis**

	Dukes A (T2,N0)	Dukes B (T3-T4,N0)	Dukes C (T3-T4, N1-N2)	TOTAL
RChT	0	14	20	34
RT	0	8	12	20
No pretreatment	64	40	30	134
TOTAL	64	62	62	188

**TABLE 2**

**Frequencies of impaired wound healing reported in ASR patients from different groups  
and the median times of their postoperative hospitalization**

	RT n=20	RChT n=34	No neoadjuvant n=134
Postoperative mortality	0 (0%) <sup>a</sup>	0 (0%) <sup>a</sup>	0 (0%) <sup>a</sup>
Superficial infection (skin only)	2 (10%) <sup>a</sup>	10 (29%) <sup>b</sup>	13 (10%) <sup>a</sup>
Deep infection (skin + subcutaneous tissue)	1 (5%) <sup>a</sup>	3 (9%) <sup>a</sup>	3 (2%) <sup>a</sup>
Abscess	0 (0%) <sup>a</sup>	1 (3%) <sup>a</sup>	2 (1%) <sup>a</sup>
Skin dehiscence + granulation	0 (0%) <sup>a</sup>	1 (3%) <sup>a</sup>	1 (1%) <sup>a</sup>
Skin dehiscence + surgical intervention	0 (0%) <sup>a</sup>	1 (3%) <sup>a</sup>	0 (0%) <sup>a</sup>
Improper wound healing in total	3 (15%) <sup>a</sup>	16 (47%) <sup>b</sup>	19 (14%) <sup>a</sup>
Perineal hernia	0 (0%) <sup>a</sup>	0 (0%) <sup>a</sup>	2 (1%) <sup>a</sup>
Median postoperative hospitalization (days)	10.5 <sup>a</sup>	11.0 <sup>a</sup>	10.0 <sup>a</sup>

<sup>a,b</sup> various superscripts indicate significant differences between the values in the rows, Fisher's exact test, Mann-Whitney U test,  $p \leq 0.05$

**TABLE 3**

**Median duration of postoperative hospitalization in lower-rectal patients with and without acute wound healing complications**

Type of complication	Complications (+)			Complications (-)		
	n	hospitalization		n	hospitalization	
		median	range		median	range
Superficial infection (skin only)	25	10 <sup>a</sup>	8-12	163		
Deep infection (skin + subcutaneous tissue)	7	12 <sup>b</sup>	9-15	181		
Abscess	3	12 <sup>b</sup>	9-16	185	10 <sup>a</sup>	7-12
Skin dehiscence + granulation	2	13 <sup>b</sup>	10-18	186		
Skin dehiscence + surgical intervention	1	13 <sup>b</sup>	–	187		
Improper wound healing in total	38	12 <sup>b</sup>	8-18	150		

<sup>a,b</sup> various superscripts indicate significant differences between the values, Mann-Whitney U test,  $p \leq 0.05$

**TABLE 4****Frequencies of local recurrences in ASR patients subjected to wound healing analysis**

	Dukes A n=64	Dukes B n=62	Dukes C n=62	TOTAL n=188
RChT (n=34)	0/0	0/14	2/20 (10.0%)	2/34 (5.9%)
RT (n=20)	0/0	0/8	0/12	0/20
No pretreatment (n=134)	0/64	3/40 (7.5%)	5/30 (16.6%)	8/134 (6.0%)
TOTAL (n=188)	0/64	3/62 (4.8%)	7/62 (11.3%)	10/188 (5.3%)