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Sphincter-Sparing Surgery in Patients with Mid and Low Rectal Cancer - Risk Factors for Local Recurrence and Anastomotic Leakage

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Abstract

Background: Rectal cancer is a major health problem. The current treatment of distal rectal cancer involves a multimodality approach aimed at achieving an optimal oncologic control and an increased quality of life.

Purpose: The purpose of this article is to identify the risk factors for local recurrence and anastomotic leakage in patients with mid and low rectal cancer who underwent sphincter-sparing surgery.

Methods: A prospective study of 38 patients with mid and low rectal cancer who underwent sphincter-sparing surgery was conducted. The patients were divided into two groups based on their tumor stage: stage I-II (n=24) and stage III-IV (n=14). The risk factors for local recurrence and anastomotic leakage were identified.

Results: The overall recurrence rate was 23.7%, with 6.3% occurring in the local recurrence group and 17.4% in the anastomotic leakage group. The risk factors for local recurrence included: tumor stage (stage III-IV, p<0.05), lymph node involvement (≥4 nodes, p<0.05), and preoperative radiotherapy (p<0.05). The risk factors for anastomotic leakage included: tumor stage (stage III-IV, p<0.05), lymph node involvement (≥4 nodes, p<0.05), and anemia (p<0.05).

Conclusion: The risk factors for local recurrence and anastomotic leakage in patients with mid and low rectal cancer who underwent sphincter-sparing surgery include tumor stage, lymph node involvement, and anemia. Preoperative radiotherapy may reduce the risk of anastomotic leakage.

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Rectal cancer is a major public health problem, it is the third most common cancer worldwide (1). The standard therapeutic strategy consists in neoadjuvant radiochemotherapy followed by surgical resection with total mesorectal excision (TME). The incidence of rectal cancer is increasing worldwide and in terms of mortality rates, rectal cancer represents the second leading cause of death among both men (11.6%) and women (13%) (2).

The surgical management was decided by a multidisciplinary team (MDT) with the work of colorectal surgeons, imagists, oncologists, radiation therapists, pathologists. The gold-standard in rectal surgery involves sharp dissection under direct vision in well-lighted field following the Heald’s “Holy Plane” and the excision of the intact unit of the rectum together with the entire mesorectum and intact perirectal fascia. The result is an oncological resected specimen R0. In this way the risk of local recurrence decreases to 10% (4).

Abdominoperineal resection is still widely performed, although having important consequences on the quality of life of these patients. The permanent stoma has major psychological impact, affecting the social reintegration, the quality of life and involves permanent stoma care.

Therefore, the improvements in mechanical suture technologies brought an essential contribution in low level rectal reconstruction. The standardization of neoadjuvant chemoradiation treatment may lead to „downstage” the tumors so the sphincter-sparing surgery can be performed even in initial locally advanced tumor stages.

Material and Method

We prospectively studied a group of 38 patients with sphincter-sparing surgery for mid and low rectal cancer at Department of General Surgery, Coltea Clinical Hospital, Bucharest, between 2012 and 2015. We included only patients with middle third and middle low rectal cancer within 9 cm from anal verge. The diagnosis was confirmed by paraffin pathology exam. Preoperative stadiation included clinical evaluation (digital rectal examination) and flexible colonoscopy with biopsy, abdominal ultrasound, chest X-ray, high-quality imaging scans (computed tomography-CT, magnetic resonance imaging-MRI). Patients have benefited of anal sphincter preservation surgery and abdominoperineal resection.

Data were analyzed prospectively, following the criteria: age, sex, tumor location, comorbidities, neoadjuvant treatment, type of surgery, presence of ileostomy, number of lymph nodes examined and the number of invaded lymph nodes, postoperative complications. Data were processed and analyzed using statistical test Chi-Square by SPSS v20 programme for Windows. A p value less than 0.05 was considered statistically significant.

Neoadjuvant therapy consisted of radiotherapy alone or in association with chemotherapy. The surgery was performed at the average interval of 4-6 weeks after completion of neoadjuvant therapy. The sphincter-sparing surgery consisted in low anterior resection (LAR) with stapled end-to-end colorectal anastomosis and ultralow anterior resection (ULAR) with hand-sewn coloanal anastomosis. Total mesorectal excision (TME) was performed for all patients.

The surgical management was decided by a multidisciplinary team (MDT) with the work of colorectal surgeons, imagists, oncologists, radiation therapists, pathologists. The inclusion criteria for sphincter-sparing surgery were: the distance from the anal verge, the histopathological stage, asso-
cated comorbidities, the surgeon’s experience in colorectal cancer surgery and the accessibility to mechanical suturing devices.

**Results**

During a period of three years we studied 38 patients diagnosed with low and mid rectal cancer who underwent sphincter-sparing surgery. We excluded patients with transanal tumor resection.

The patients characteristics are presented in Table 1. The list of comorbidities included cardiovascular diseases such as hypertension (29 cases, 76.3%), ischemic heart disease (23 cases, 60.5%), heart failure (24 cases, 63.2%), diabetes mellitus type II (7 cases, 18.4%), dyslipidemia (7 cases, 18.4%). The clinical TNM stages included T1 and T2 stage cancers in 36.8% of patients (14 cases), and T3 stage tumors in 24 cases (63.2%). Of all cases in the study, 2 patients (5.3%) benefited from temporary colostoma so the neoadjuvant therapy can be followed. These two patients underwent low anterior resection. One patient developed tumor recurrence 2 years later and required abdominoperineal resection.

Neoadjuvant therapy was applied in selected cases. Most patients (33 cases, 86.8%) received external beam radiation (EBR) with conventional fraction of 45-50 Gy with administration of 1.8-2 Gy/session. Half the patients have had associated neoadjuvant chemotherapy.

Surgery was performed 4-6 weeks after completion of neoadjuvant treatment. The surgical therapeutic options included: low anterior rectal resection (LAR) with end-to-end colorectal anastomosis using circular staplers in 32 cases (84.2%) and ultralow anterior rectal resection (ULAR) followed by coloanal anastomosis in 6 cases (15.8%) (Table 2). Total mesorectal excision (TME) was performed in all cases. The resected rectum was a cilinder shape specimen with glossy, intact mesorectum and perirectal fascia.

The surgeons used linear staplers for resection of the rectum and colon and circular end-to-end anastomosis (EEA) staplers for colorectal anastomosis. The integrity of the anastomosis was checked by transanal air or methylene blue instillation. There were only few cases (2 patients, 5.2%) which had required staple line reinforcement using one or two sutures 2.0 or 3.0. The resected specimen was examined ex-vivo with a special devices.

The statistical analysis revealed an association between the complications rate and neoadjuvant radiotherapy (50% in the preoperative radiotherapy group compared with 7.9% in the group without radiotherapy). There is a similar association in case of preoperative chemotherapy (31.6% vs. 26.3%). There is a significant association between anemia and the complication rate. Preoperative hemoglobin level above 11 g/dL is a protective factor against the development of postoperative complications (42.1%, p=0.03). Postoperative hemoglobin below 11 g/dL is associated with higher rates of complications (47.4%, p=0.05). Tumor markers carbohydrate antigen CA 19-9 and carcinoembryonic antigen CEA have not been significantly associated with complication rate, but CA 19-9 level was increased mostly in T3 stage cancers, p=0.001.

Pathologist examined an average number of lymph nodes excised of 12.7 (maximum 50 lymph nodes per specimen), and identified an average number of positive nodes of 2.9 (maximum 46 lymph nodes per specimen).

We identified 20 cases (52.6%) with postoperative complications. We have observed an association between advanced TNM stage and the complication rate (44.7% for stage T3 cancers, p=0.05).

Anastomotic leakage (AL)

After restorative rectal resection 4 patients (10.5%) developed grade B anastomotic leakage (AL) (according to International Study Group of Rectal Cancer) (5). In case of these 4 patients with AL we found these following data. Due to the anatomical difficulties, there were more cases in men than in women (3

<table>
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<tr>
<th>Table 1. Distribution according to sex, age, tumor location, AJCC (American Joint Committee on Cancer) cancer stage</th>
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<td><strong>Age</strong></td>
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<td><strong>Rectum</strong></td>
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<td><strong>Stage I</strong></td>
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<td><strong>Stage II B</strong></td>
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<td>T3 T4 N1 M0</td>
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<td>Any T N2 M0</td>
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<td><strong>Stage IV</strong></td>
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<th>Table 2. Type of surgery and ileostomy rate distribution</th>
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<td><strong>Type of surgery</strong></td>
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<td><strong>Ileostomy</strong></td>
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Local recurrence (LR)

The recurrence rate (LR) was 7.9% (3 cases) and it was associated with TNM stage T3 cancers and the number of positive lymph nodes (more than 4 nodes, 5.3%, p=0.023). The initial tumor was located at the middle rectum in 2 cases and at the inferior rectum in 1 case. Tumor markers carbohydrate antigen CA 19-9 (3 cases) and carcinoembryonic antigen CEA (2 cases) level have been increased. Two patients with LR had underwent neoadjuvant radiochemotherapy.

Local recurrence has developed on an average of 2 years (minimum 1 year, maximum 3 years) after the initial surgery. One of the three cases developed local recurrence at 1 year after restorative rectal resection for T3N0M0 stage cancer. The patient underwent radical surgery with permanent stoma, but after another 1 year he developed another local relapse (tumoral invasion of the presacral fascia) which led to an R2 resection. The second patient developed a local recurrence at 3 year after rectal resection for T3N2M0 stage cancer. The surgical option was limited to exploratory laparotomy with permanent colostomy. In the third case the local recurrence was discovered by a follow-up colonoscopy examination. The patient had major comorbid conditions (liver and bone metastasis, cardiac failure, renal chronic failure, intracerebral tumor, ureterohydronefrosis and deep left vein thrombosis due to left piriiform muscle and dorsolateral tumor involvement of the pelvis) that left no option for radical surgery. He underwent palliative therapy. The pathology examination revealed that LR occurred in 2 cases of moderate-differentiated adenocarcinoma and in 1 case of well-differentiated adenocarcinoma. There were no evidence of serous tumor involvement nor perineural and lymphovascular invasion in all LR cases, but the radial margin invasion was found in 1 case. All three patients have developed postoperative anemia. Postoperative chemotherapy was applied for all 3 patients and only 1 patient have had associated external radiotherapy.

A number of other complication was identified: bowel obstruction due to adhesions or bowel volvulus (5 cases, 13.2%), prostatodytology colitis (3 cases, 7.7%), coloanal anastomotic stenosis (1 case, 2.6%), rectovaginal fistula (1 case, 2.6%), ileostomy bleeding (1 case, 2.6%), wound infection (2 cases, 5.3%). The mortality rate was 5.26% (2 cases). One patient who benefited of restorative rectal resection having major cardiovascular and neurologic comorbidities died during the 10th postoperative day due to an intestinal dynamic obstruction. Another patient died after intestinal obstruction by adhesions at 1 year after anterior resection (patient with BMI more than 26 and major cardiovascular comorbidities).

The quality of life of these patients was assessed by a subjective analysis according to the clinical complaints, digestive tolerance, bowel and urogenital function, postoperative anal continence, level of family, social and professional work reintegration. The absence of permanent colostomy had a favorable impact on the normal digestive functionality and postoperative evolution. We identified a good quality of life, with favorable postoperative evolution, encumbered by a reduced number and intensity of surgery-related complications.

The current article is limited by the small number of the patients included in study. The analysis is based on highly variable factors like surgeon-related factors (extended experience in colorectal surgery) and patient-related factors (tumor stage, pathology exams, tumor location, age, comorbidities, neoadjuvant chemoradiotherapy, type of surgery, presence of ileostomy, patient’s decision). The patient was given the consent and his decision was an important factor. Although it is a subjective criteria, the patient with absolute refusal for permanent stoma, despite the MDT’s recommendations, resulted in still limited oncological radicality. In exceptional cases there were performed rectal resections with colorectal anastomosis for tumor stage T3 cancers.

Discussions

Colorectal cancer incidence is still increasing, both in women and men (1,2). Worldwide, rectal cancer is the third most frequent of all cancers and a leading cause of overall mortality (6). Relative incidence of rectal cancer increases with age. There are theories that are involving the role of lifestyle-related obesity and dietary imbalances. The risk factors may increase with age. The chances of genetic mutation or malignant transformation of colorectal adenomas and polips is directly proportional with age.

Multimodality treatment will provide an optimal oncologic outcome along with a favorable prognostic and long-term survival. Despite the remarkable technological developments in mechanical suturing devices the surgical treatment of distal rectal cancer remains a challenge.

A combination of external irradiation with neoadjuvant chemotherapy has been shown to achieve significant survival benefits by „downstaging“ the tumor and by improving reseca-
Sphincter-sparing surgery for distal rectal cancer has low rate of local recurrence and anastomotic leakage. The risk factors for both local recurrence and anastomotic leakage are aggressive tumor stages, lymph-node tumor invasion, postoperative anemia and neoadjuvant therapy. The mortality rate is also low after sphincter-sparing surgery. The introduction of national screening programs in high risk individuals will increase the prognosis of rectal cancer by improved early diagnosis and wide range sphincter-sparing surgery.

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