LOW-AntERIOR-RESECTIOn SYNdROmE. HOW DOES NEOADJUVANT RADIOTHERAPY AND LOW RESECTIOn OF THE RECTUM INFLUENCE THE FUNCTION OF ANAL SPHINCTERS IN PATIENTS WITH RECTAL CANCER? PRELIMINARY RESULTS OF A FUNCTIONAL ASSESSMENT STUDY*

MICHAŁ ROMANISZYN, PIOTR RICHTER, PIOTR WALEGA, JAKUB KENIG, MARCIN NOWAK, WOJCIECH NOWAK

3rd Department of General Surgery, Jagiellonian University Collegium Medicum in Cracow
Kierownik: prof. dr hab. W. Nowak

The aim of the study was to assess the influence of neoadjuvant radiotherapy and resection of the rectum on the functional parameters of anal sphincters.

Material and methods. 20 patients with rectal cancer, qualified for low anterior rectal resection with neoadjuvant radiotherapy were enrolled in the study group. The study protocol included an anorectal manometry, electromyography and fecal incontinence questionnaire (FISI) before radiotherapy, after radiotherapy, and after the operation.

Results. Of the 20 patients 12 were included in the final analysis, because 8 patients were re-qualified to abdomino-perineal resection of the rectum after neoadjuvant treatment. There were no significant changes in anal pressures assessed 5 to 8 days after radiotherapy. In 3 cases (25%) pathological changes in RAIR reflex were found in the manometric examination. After low anterior resection mean basal anal pressures were significantly lower, whereas squeeze anal pressures did not change significantly. In 7 patients (58%) the RAIR reflex was pathological or even absent after low anterior resection. Changes in manometric parameters correlated with FISI incontinence assessment after the operation. In electromyographic examination action potentials of motoric units of the external anal sphincter were still present both after radiotherapy, and after operation.

Conclusions. Fecal incontinence after low anterior resection of the rectum seems to be caused mostly by changes in autonomic functionality of anal sphincters and lack of compliance of the neorectum, since the influence of neoadjuvant radiotherapy and the operation itself on the somatic innervation of anal sphincters seems to be minimal.

Key words: rectal cancer, low anterior resection, neoadjuvant radiotherapy, anal sphincter function

Fecal incontinence is a common disorder after anterior rectal resections due to rectal cancer (ranging from 10 to 60%), despite the initial claims, that the risk of sphincter dysfunction after sphincter-saving rectal resections is minimal (1). Moreover, studies show that in patients with neoadjuvant radiotherapy the risk of fecal incontinence after operation is even greater, although it is still not clear, what is the exact pathophysiological mechanism of this disorder (2). It is a well known fact, that irradiation of the pelvis, apart from affecting the tumor cells, causes destruction of vulnerable structures in the direct vicinity of the rectum – including the muscle tissue of the anal sphincters and nerve fibers innervating the sphincters and rectum. The destructive effect of the radiation apparently adds up to potential damage of pelvic nerves during total mesorectal excision, and increases the risk of so called “Anterior Resection Syndrome” even if nerve-sparing techniques are used. The most common symptoms of the “Anterior Resection Syndrome” are listed in tab. 1.

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The damage done by the radiation to the sphincter muscle itself seems to be a secondary issue, since in 10-60% (4, 5) of cases anal sphincter dysfunction is accompanied by urinary and sexual disorders (hyperactive bladder, urine incontinence, urine retention, impotence, lack of ejaculation, lack of orgasm), which points towards a neurological etiology of the disorder, whereas isolated fecal incontinence after radiotherapy is rather rare.

The anal sphincters are innervated by many neural fibers, branches and bundles, including pudendal nerve, pelvic splanchnic nerves and hypogastric nerves forming the pelvic plexus, and also the neurovascular bundle (6). These nerves contain autonomic and somatic components (the pudendal nerve contains fibers of all three systems: sympathetic, parasympathetic and somatic (7), which regulate the function of the anorectal complex not only by allowing voluntary contraction of the sphincter through somatic impulsion, but also by managing complex autonomic anorectal reflexes and internal anal sphincter function.

It is being widely discussed in the literature which factor is the most responsible for the “Anterior Resection Syndrome” – damage of autonomic fibers, somatic component or just the consequences of excision of the rectum and subsequent lack of compliance of the neo-rectum, and it is commonly agreed that concerning damage done to neural structures, dysfunction of the autonomic fibers affects the sphincter function the most (8). This assumption is mostly based on manometric analyzes of sphincter function, since diagnostic tests to directly assess neural conductivity are either difficult to perform or inconvenient for the patients, and are not routinely performed. However, only recently a tool has been developed, which allows convenient routine assessment of somatic innervation of the sphincters and thus the possibility to exclude one of the factors from the equation. The assessment of somatic innervation of the external anal sphincter can be safely and easily done by the means of surface electromyography (9).

Moreover, the effect of neoadjuvant radiotherapy on the pathophysiology of “Anterior Rectal Resection” – concerning neurophysiology – can also be assessed using surface electromyography, and it is also a point of interest of several studies (10).

The aim of this study was to present preliminary results of neurophysiological assessment of the influence of neoadjuvant radiotherapy and resection of the rectum on anal sphincters.

**MATERIAL AND METHODS**

20 patients with rectal cancer, qualified for low anterior rectal resection with neoadjuvant radiotherapy were enrolled in the study group.

The study group inclusion and exclusion criteria are listed below:

**Inclusion criteria:**
- age 18-85,
- histopathologically confirmed adenocarcinoma of the rectum,
- stage II or III of the disease, qualified for neoadjuvant radiotherapy,
- tumor localized up to 8cm from the anal verge.

**Exclusion criteria:**
- age below 18 or above 85,
- stage IV of the disease,
- infiltration of the sphincters,
- diabetes with neuropathy, or any other neurological conditions,
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– sphincter dysfunction due to earlier colorectal procedures,
– other colorectal co-morbidities (advanced hemorrhoidal disease, fistulas, fissures etc).

The study protocol included an anorectal manometry, electromyography and fecal incontinence questionnaire (FISI) before radiotherapy, after radiotherapy, and third assessment – after the operation. Each patient had a manometric examination performed, using a 4-channel air-charged micro-balloon catheter (fig. 1), and following parameters were recorded: mean basal pressure (BAP), maximum squeeze pressure (SAP), rectoanal inhibitory reflex (RAIR), cough reflex (RSCC) and rectal sensation volumes (first sensation – FS, First Urge to defecate – FUTD, Maximum Tolerable Volume – MTV) (fig. 2).

The electromyographic examination was performed using a 48-channel 3-ring rectal probe (fig. 3), the signal was analyzed to assess the presence and morphology of motor units action potentials. Waves of potentials propagating from innervation zones (as in fig. 4) were considered as “normal external sphincter somatic innervation”, whereas lack of those, or if the signal consisted of uncoordinated action potentials, the recording was considered as “external sphincter somatic innervation disturbances”.

Fecal incontinence assessment was made using a standardized FISI questionnaire.

Patients were qualified for neoadjuvant radiotherapy according to 5-day protocol – 5 days of irradiation, with 5 Gy each day to a total dose of 25 Gy. The second functional assessment was performed 5 to 8 days after the last dose of irradiation. Then, after restaging, patients were qualified for surgery.

RESULTS

Of the initial 20 patients only 11 were included in the final analysis, because 9 patients were re-qualified to abdomino-perineal resection of the rectum after neoadjuvant treatment, or had complications after the operation, and thus were excluded from the study.

There were no significant changes in anal pressures assessed 5 to 8 days after radiotherapy compared to pressures before irradiation. In 3 cases (27%) pathological changes in RAIR reflex were found in the manometric examination. After low anterior resection mean basal anal pressures were significantly lower, whereas squeeze anal pressures did not change significantly (fig. 5, 6).
In 7 patients (63%) the RAIR reflex was pathological or even absent after low anterior resection. Changes in manometric parameters correlated with FISI incontinence assessment after the operation, however the correlation was not significant (p>0.05) (fig. 7).

In electromyographic examination action potentials of motoric units of the external anal sphincter were still present both after radiotherapy, and after operation, with proper morphology and propagation in all patients. There no cases of missing signals from pudendal nerves (count of innervation zones before, after radiotherapy and after the operation was the same in all cases).
DISCUSSION

This paper presents preliminary results of neurophysiological assessment of anorectal function after anterior resection of the rectum preceded by neoadjuvant radiotherapy. There were several studies concerning functional results after such multimodal therapy, and their results are often contradictory, since some studies blame surgery as the only factor responsible for the Anterior Resection Syndrome, regardless of other kinds of therapy involved (11), whereas in many studies multimodal treatment of rectal cancer compared with surgery alone results show that radiotherapy indeed increases the risk of fecal incontinence after treatment (12). The results of our study show that patients after anterior resection of the rectum with neoadjuvant radiotherapy do often suffer from fecal incontinence, but since there was no control group without radiotherapy analyzed, it is difficult to distinguish, whether radiotherapy worsened functional results after surgery – it was not however the main goal of this study.

Most researchers agree, that fecal incontinence after Anterior Resections of the Rectum is a condition influenced by many factors (13, 14). In patients suffering from Anterior Rese-ction Syndrome the severity of symptoms is said to be influenced mostly by basal tone of the sphincter apparatus, it’s ability to generate voluntary contraction, recto-anal reflexes (sampling reflex, recto-anal inhibitory reflex), reservoir capacity of the neo-rectum determined by length of the rectal stump and surgical technique. Anorectal manometry can be used to assess sphincter pressures and anorectal reflexes, as well as reservoir capacity, aided by balloon tests or barostatic examinations, but one must remember that anorectal function parameters are secondary to several variables, determined by different parts of autonomic and somatic nervous systems.

As far as anorectal manometry is concerned, it is a well known tool for assessment of anorectal functions in various conditions (15), including the assessment after surgical procedures and radiotherapy. In most publications it is shown that patients with fecal continence impairment have lower anorectal pressures (16) or disturbances in anorectal reflexes (17). However, in several publications results showed no significant correlation between manometric parameters and degree of fecal incontinence (17, 18). Preliminary results of our study also show no significant correlation between manometric parameters and FISI score, this might however be due to small sample size, so it is not determinative so far. What is more important in this matter, each of the manometric pressures is composed of several elements. Voluntary squeeze pressure, determined mostly by the external sphincter’s

Table 2. Demographic data

<table>
<thead>
<tr>
<th>Male/female ratio</th>
<th>7:4</th>
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<tbody>
<tr>
<td>Mean age</td>
<td>66</td>
</tr>
<tr>
<td>Median age</td>
<td>63</td>
</tr>
<tr>
<td>Mean anastomosis level</td>
<td>4 (cm from the verge of anus)</td>
</tr>
</tbody>
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Table 3. Mean values in functional assessments

<table>
<thead>
<tr>
<th></th>
<th>Initial values</th>
<th>Post-RTGth</th>
<th>Post-operative</th>
</tr>
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<tbody>
<tr>
<td>BAP (mm Hg)</td>
<td>52.27</td>
<td>49.73</td>
<td>40.73</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>178</td>
<td>167</td>
<td>159</td>
</tr>
<tr>
<td>RAIR pathology (n)</td>
<td>0</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>sEMG signal loss (n)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
ability to contract in response to somatic im-
pulsation, is said to be less important in the
Anterior Resection pathogenesis. Basal sphin-
cter pressure on the other hand, consists of
pressures generated by the internal anal
sphincter (approx. 40-60%), external anal
sphincter (about 20-50%) (19), and hemor-
rhoidal cushions, so three components are
involved: autonomic and somatic innervation,
as well as anatomical structures within the
anal canal. Rectal examination and anoscopy
can exclude anatomical disturbances of the
anal canal as causes of lower basal pressure,
but still the influence of both neurological
systems remains in the terms of statistics. So
in this study, an additional test was used –
electromyography of external anal sphincter.
This tool allows complex analysis of external
sphincter’s innervation, as proven in previous
studies (9, 10).

In this study, the presence and morphology
of the EMG signal was analyzed showing no
major changes concerning propagation of mo-
toric unit action potentials and innervation
zones, meaning that the somatic components
of pudendal nerves were not destroyed during
irradiation and surgery. The preliminary re-
sults of this study are promising and may lead
to certain benefits for patients in future. How-
ever, a more detailed analysis of this complex
neuromechanical apparatus of anal sphincters
is required on a larger group of patients.

CONCLUSIONS

Fecal incontinence after low anterior resec-
tion of the rectum with neoadjuvant radio-
therapy seems to be caused mostly by changes
in autonomic functionality of anal sphincters
and lack of compliance of the neorectum, since
the influence of neoadjuvant radiotherapy and
the operation itself on the somatic innervation
of anal sphincters seems to be minimal. It is
yet to be researched in comparative case con-
trolled studies, to what degree the adverse
effects of neoadjuvant radiotherapy add up to
the risk of fecal incontinence after anterior
resection of the rectum.

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Address correspondence: 31-202 Kraków, ul. Prądnicka 35 – 37