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Rectal tumor recurrence: What more may we learn?

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ABSTRACT

Background: Notwithstanding real progress in the treatment of rectal cancers, local recurrence remains a challenging problem. We performed a retrospective observational study focusing on anatomo-surgical data.

Methods: In our retrospective study, we adopted new morphological classifications of primary tumor downstaging, after neoadjuvant treatment, and of local recurrence of rectal cancers, mainly based on CT and MRI images.

Results: Different risk factors of rectal cancer recurrence were identified: its initial advanced stage, its high histological grading, and its non-responsiveness to neoadjuvant treatment. In addition, particular anatomo-surgical points have been underlined, mainly focused on the total mesorectal excision.

Conclusions: We reaffirmed the value of a correct surgical technique, although other aspects of this disease demand further research.

Key words: *Rectal cancer, recurrent, computed tomography, mesorectal excision, neoadjuvant radio-chemotherapy*

Introduction

In recent years, the recurrence of rectal cancer has been reduced, due to adjuvant or neoadjuvant treatments and to improved surgical techniques [1]. Nevertheless, this cancer still represents a challenge for surgeons. Today, its diagnosis is greatly facilitated by modern cross-sectional imaging techniques, ultrasound (US) , contrast-enhanced computed tomography (CT), magnetic resonance (MR) , and positron emission tomography (PET), which usually complete the clinical and endoscopic examinations. The aim of our retrospective observational study was to evaluate the importance of imaging tools, particularly CT, for the diagnosis of this disease, as well as to investigate which anatomo-surgical factors predispose patients to the recurrence of rectal cancers.

Patients and Methods

Inclusion criteria

We performed a retrospective study with 38 patients (29 males and 9 females) aged between 60 and 75 years old, observed at our Institution in between 2010 and 2014, where a sure diagnosis of locally-recurrent rectal cancer was proved by histology. We considered only cases free of distant metastases and without neoplastic positive resectional or circumferential margins at the first surgery. This last condition was considered a persistent, rather than a recurrent, neoplastic disease.

In all our cases, the initial tumor was located in the

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lower or middle rectum, within 10 cm of the anorectal junction. The initial staging always corresponded to T3, and to N0 in 8 cases, N1 in 16, and N2 in 14; histological grading corresponded to G2 in 27 cases and G3 in 11. All patients had a neo-adjuvant radio-therapy of 50 Grays associated with a FOLFOX pharmacological treatment; surgery followed after 5-6 weeks. The histopathological regression of the primitive tumor after neo-adjuvant radio-chemotherapy, classified according to the Dworak score in the surgical specimen, was graded as 0 in 5 cases, 1 in 25, and 2 in 8 [2,3].

The clinical study of our patients was performed according to the ESMO guidelines [4] and included clinical examinations, colonoscopy, abdominal US, and CT, which is usually the preferred first imaging tool for a complete study of the thorax, abdomen, and pelvis [5,6].

In order to evaluate rectal tumor regression after the first neo-adjuvant radio-chemotherapy, we adopted the following classification, based on cross-sectional images, CT, and MR (Table 1):

Grade 0: unchanged feature of the rectal tumor (11 cases)

Grade 1: partial regression of the sole mesorectal infiltration (17 cases)

Grade 2: partial regression of the mesorectal and rectal wall neoplastic infiltration (10 cases).

Results

The most common CT characteristics observed in case of rectal cancer recurrence can be summarized as follows: a simple thickness of the colorectal wall, often corresponding to the anastomotic site and demanding a further endoscopic control; an unique dense pelvic mass or multiple nodules, typically with an irregular shape and speculated margins in the residual mesorectum or involving the pelvic or perineal muscles and spaces, or the neighbouring organs, sometimes with a superimposed fistula. Moreover, the pelvic bones, the iliac fossae, and the proximal intra-peritoneal spaces can be infiltrated by neoplastic tissue (Figure 1-3).

Classification of recurrent rectal cancer

From a simple topographical point of view, recurrences of rectal cancer are usually classified as: central, often discovered endoscopically, concerning the colorectal walls, and often corresponding to the anastomosis site; anterior, posterior, or lateral, in relation to colorectal walls, when an anastomosis had been performed, or within the residual pelvic space in case of abdominoperineal resection; or diffuse when contemporarily involving two or more pelvic spaces.

In addition, we performed a classification of the grade of local rectal tumor recurrence, based on anatomo-radiological criteria (Table 2):

Grade 1: colorectal parietal recurrence (3 cases)

Grade 2: colorectal parietal recurrence and/or involvement of the residual mesorectum (4 cases)

Grade 3: colorectal parietal recurrence and/or involvement of the anterior pelvic organs (prostate, bladder, vagina), or mono-laterally to the perineal muscles (16 cases)

Grade 4: colorectal parietal recurrence with involvement of the pelvic organs and/or of the pelvic fascia or sacrum, or bilaterally to the perineal muscles or one or both of the iliac fossae (15 cases).

We observed that the grades of tumor downstaging after the first neo-adjuvant treatment correlated inversely with severity of tumor recurrence in 35 cases (92.10%), but correlated directly with the Dworak histopathological regression in 28 cases (73.68%). Similarly, early recurrence typically corresponded to a low grade of regression after neoadjuvant treatment (Grade 0 and 1) and to a poor Dworak score (Grade 0 and 1).

Considering the delay of rectal tumor recurrence,

Table 1. Grades of tumor regression after neoadjuvant radio-chemotherapy.

0	unchanged feature of the rectal tumor
1	partial regression of the sole mesorectal infiltration
2	partial regression of the mesorectal and rectal wall neoplastic infiltration
3	Regression, complete of mesorectum, partial of rectal wall
4	Complete disappearance of the rectal tumor

Table 2. Grades of tumor recurrence.

1	colorectal parietal recurrence
2	colorectal parietal recurrence and/or involvement of the residual mesorectum
3	colorectal parietal recurrence and/or involvement of the anterior pelvic organs (prostate, bladder, vagina), or mono-laterally to the perineal muscles
4	colorectal parietal recurrence with involvement of the pelvic organs and/or of the pelvic fascia or sacrum, or bilaterally to the perineal muscles or one or both of the iliac fossae

Figure 1. CT axial scans of patients with rectal cancer. **(A)** the anterior rectal wall is irregularly thickened (arrow), and the right anterior mesorectum is infiltrated. **(B)** recurrent rectal cancer (arrow), largely expanding in the anterior mesorectum, and infiltrating the rectal wall and the pelvic fascia. **(C)** recurrent rectal cancer largely infiltrating the anterior mesorectum and the pelvic left lateral wall. **(D)** recurrent rectal cancer massively infiltrating the anterior pelvis.

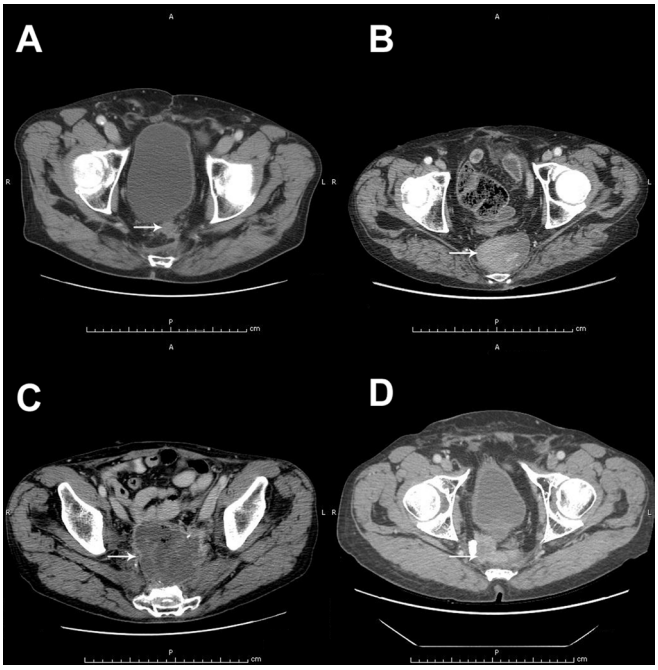

Figure 2. CT axial scans of patients with rectal cancer after abdominoperineal resection. **(A)** limited nodular infiltration of the posterior mesorectum (arrow). **(B)** extended neoplastic mass in the posterior pelvis (arrow). **(C)** large neoplastic mass infiltrating the posterior pelvis and extending to the pro-peritoneal space (arrow). **(D)** neoplastic mass infiltrating the posterior and left lateral pelvis (arrow).

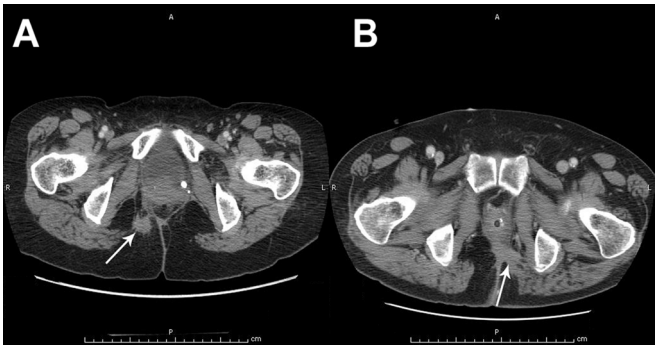

Figure 3. CT axial scans of patients with rectal cancer after abdominoperineal resection. **(A)** a speculated neoplastic mass in the right perineum (arrow). **(B)** neoplastic mass infiltrating the left perineum and the gluteus maximus muscle (arrow).

we distinguished an early recurrence as appearing within 6 months (24 cases), a mid-term recurrence as being observed within 12 months (5 cases), and a late recurrence as being observed after 1 year (9 cases). Obviously, the time before discovery of rectal tumor recurrence cannot always be considered to correspond with its real onset, but it can also depend on the scheduled intervals of time of the follow-up.

Discussion

Our single-institution review, with its small sample size, did not allow for certain statistical studies. Morphological evaluation of our cases was mainly based on CT images, as this technique is the most widely used as a first radiological approach. It can be followed by other more sophisticated radiological examinations, such as MRI and PET. Radiological imaging does not always have an absolute value, however, because sometimes features of a recurrent neoplastic disease can be similar to a secondary fibro-inflammatory reaction to radiation or surgery. Similarly, the difference between neoplastic involved and simply reactive lymph-nodes can be elusive [7,8].

In our study, we introduced classifications of tumor regression after a neoadjuvant treatment and of severity of recurrence, based on clinico-radiological elements. Our classifications must now be validated by further studies (Tables 1 and 2).

Some anatomo-surgical observations appear interesting. Firstly, the mesorectum must be considered a unique anatomical entity, possessing an abundant and well developed lymphatic network and connected with the lymphatic capillaries of the rectal submucosa. True valves are not visible at the conventional histology in the mesorectal lymphatic capillaries and collectors. This suggests a possible bidirectional up- and downstream lymphatic flow in the mesorectum, especially in cases of superimposed inflammation, previous radio-

therapy, or neoplastic infiltration. Neoplastic cells, already present in the lymphatic capillaries or implanted after surgical manipulations in the mesorectal connective-adipose tissue, can migrate toward the colorectal anastomosis, where an increased vascularization favors their implant [9].

Secondly, in case of tumors infiltrating the anterior rectal wall, thinning of the anterior mesorectum represents an indication to neoadjuvant treatment, and, at surgery, to its dissection in front of the Denonvilliers' fascia [10-12]. Thirdly, in the mesorectum, the sub-fascial lymphatic network is well represented and at surgery, disruption of the mesorectal fascia must be avoided [13-15]. Moreover, after radiotherapy the pelvic posterior and the mesorectal fasciae can become strictly adherent. In this case, the surgical plane of dissection must follow the posterior parietal pelvic space and not enter the mesorectal fascia, carefully avoiding damage to the pelvic nerves and the pre-sacral venous plexuses [13].

Fourthly, total mesorectal excision does not compromise the arterial vascular supply to the rectal stump, as the inferior and not the middle hemorrhoidal artery is its most important source of blood supply [9].

Fifthly, in case of abdominoperineal resection, the total mesorectal excision must be associated to an extended perineal dissection. Sixthly, the mesorectum is not anatomically separated from the retroperitoneum of the left iliac fossa, making neoplastic diffusion towards this region possible, directly or through lymphatic connections. In case of upper rectal tumors, an associated sigmoidectomy with mesenteric resection and central vascular ligation is therefore indicated.

In addition to these surgical observations, we must consider pitfalls that are possible when re-staging rectal cancers after a neoadjuvant treatment.

An apparent and misleading downstaging or downsizing of the tumor can erroneously induce us to change the surgical strategy that was initially decided upon [16-21]. The knowledge of the intrinsic risks of recurrence of a rectal cancer must also guide the scheduling of the follow-up [22-25].

Study limitations and conclusions

Surgeons must be alerted to the problem of recurrence of rectal cancers, detecting the predisposing factors of each case and keeping their technical skills updated. Extended research will be necessary concerning particular characteristics of rectal cancer, different responsiveness to radio-chemotherapy, lymphovascular invasiveness, and systemic or local immunological reaction [26-32]. Similarly, other points, such as the real value of repeated radiotherapy or salvage surgery, demand further studies [33].

Conflict of interest statement

The authors have no conflict of interest to declare.

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