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ON THE ROLE OF RADIOLOGISTS IN THE BELGIAN PROJECT ON CANCER OF THE RECTUM, PROCARE

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Radiologists are involved at all stages of the treatment of patients with rectum cancer: in the preoperative staging, in the diagnosis of postoperative complications, in the detection of recurrent or metastatic disease during follow-up, in the monitoring of the therapeutic effect of palliative therapy.
PROCARE is a Belgian national project to improve outcome in all patients with rectum cancer. Guidelines were made by a multidisciplinary workgroup and are available on the web. Decentralised implementation of guidelines is organised by the scientific and professional organisations. It is planned that a central review committee of radiologists, delegated by the Royal Belgian Society of Radiology, will survey the quality of preoperative staging. Overall quality of care will be assured by registration in a specific national database starting in 2006. Participating teams will receive annual feedback.
Radiologists should provide data on cTNM staging and cCRM. Differentiation between cT2 and cT3, cN0 and cN+, and measurement of the cCRM in mm are crucial as they have a relevant impact on treatment strategy. While spiral abdominal CT is adequate for cM staging, high-resolution MRI is highly recommended and, in fact, a necessity for locoregional staging because its adequacy is superior to that of CT-scan and EUS. However, EUS is mandatory when local excision is considered, i.e. for cT1N0 lesions.

Key-words: Rectum cancer – Staging – Quality of care – Audit.

Each year, 1500-1600 patients present with rectal carcinoma in Belgium. They are treated by approximately 113 teams (hospitals). PROCARE is a Belgian PROject on CAncer of the REctum, aiming to improve the outcome of rectal cancer treatment by reducing the variability of the quality of care. It was initiated because several nationwide projects or audits and multicentre studies, in which TME training (total mesorectal excision) and/or (neo)adjuvant radio(chemo)therapy played a major role, had documented the feasibility and efficacy of such a project e.g. in Sweden (1, 2), the Netherlands (3, 4), Norway (5), Denmark (6), Germany (7), Poland (8). These projects/studies involved patients with resectable rectum cancer only. In contrast, the Belgian project concerns all patients, whatever the extent of their disease.

A multidisciplinary workgroup, representing all scientific organisations with an interest in the treatment of rectal cancer, as well as the professional association and the National Cancer Registry, started its activities in 2004. The project was conceived to be developed in three steps: standardisation through guidelines, implementation of guidelines, quality assurance through registration.

Multidisciplinary guidelines were finalised in November 2004 to be put on the website of the respective scientific organisations (e.g. www.belsurg.org/organisations.html under Section of Colorectal Surgery). The MOC chairmen and medical directors of the 113 hospitals in which patients with rectal cancer are treated have been and will be (re)informed about the project, its concept and guidelines. During 2004-2005, the project was presented and discussed in several LOK/GLEM groups as well as at multiple postgraduate courses, scientific meetings and seminars (Belgian Section of Colorectal Surgery, Digestive Pathology Club, Vlaamse Vereniging voor Gastroenterologie, Belgian Society of Radiotherapy – Oncology). The pathologists made a CD-rom and the radiotherapeutists an atlas for instruction. Heald R and Quirke Ph, world leaders in TME surgery and its pathological evaluation, participated in two workshops with live demonstrations and are prepared to further support the project. In 2006, information will continue targeting individual colleagues and teams through Newsletters and regional work sessions to be organised by the Belgian Professional Association in collaboration with the PROCARE workgroup and the scientific societies.

Taking into account the organisation of Belgian health care and patient rights, PROCARE has opted for a decentralised implementation of the guidelines through training/instruction of all interested teams. Indeed, participation in PROCARE will be based on a voluntary basis. If financial support from the Ministry of Health will be available in 2006, decentralised surgical and pathology instruction will be provided in 5 consecutive cases per centre for those who want to receive it. In contrast, preoperative staging and radiotherapy will be organised through a central scientific review committee of radiologists and radiotherapeutists, respectively. Surgeons that are candidate-instructor started registration at the National Cancer Registry (NCR) of consecutive TME cases in October 2005. To be quali-

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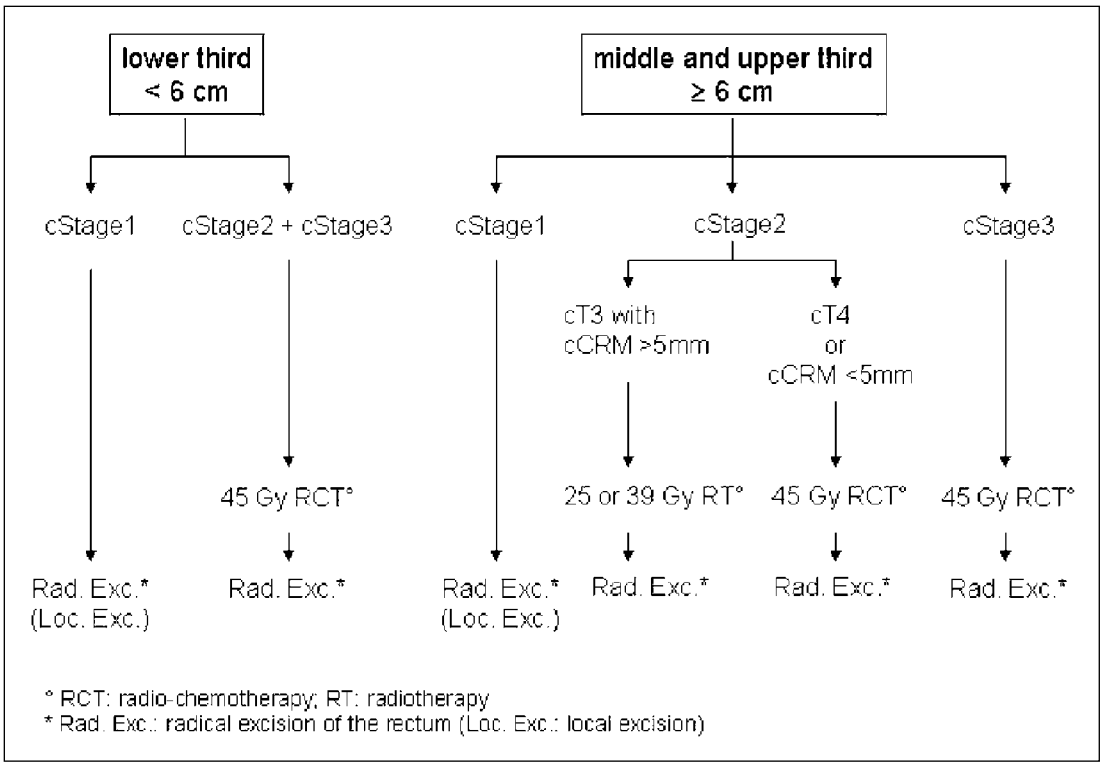

Fig. 1. — Therapeutic algorithm illustrating the key-role of preoperative staging in the treatment of resectable rectum cancer (from PROCARE Multidisciplinary Guidelines for the treatment of Rectal Cancer).

fied, a list of preset criteria must be fulfilled; the anonymous records will be evaluated by the scientific committee of the Belgian Section of Colorectal Surgery. Qualified instructors are committed to instruct all other teams in 2006 and beyond, as needed. However, surgeons who would prefer not to be instructed and perform surgery as before or by peer-to-peer collaboration, are also welcome to participate in the project by prospective registration of their patients.

Quality assurance will be based on centralised registration at the National Cancer Registry of consecutive patients. After receipt, all data are immediately anonymised and entered in a specific database. The PROCARE workgroup finalised the data entry set in 2005. Prospective registration from all centres is planned to start in January 2006. Regular feedback will be provided through Newsletters, and teams who participate in the project will receive annual feedback on their performance as compared with national data.

The potential benefit of the PROCARE project has been estimated on the basis of an analysis of the outcome in patients with rectal cancer treated in 1997-1998. The results of this retrospective study will be published in 2006. Comparison with recent trials indicate that survival in resectable rectal cancer may be improved with an absolute percentage of about 20%, while the median and 2-year survival can almost be doubled in patients with metastatic disease.

The impact of imaging on the therapeutic strategy in resectable rectal cancer

Pre-treatment diagnosis and clinical classification, cTNM, are based on clinical examination, total colonoscopy with biopsy, imaging, and, ultimately, surgical exploration. If total colonoscopy is judged to be too risky or if it is refused, a high quality double contrast barium enema or 3D virtual colonoscopy should be performed. Preoperative staging is mandatory unless it would not alter management. It should include: CEA serum level, clinical examination (fixity of palpable tumours, rigid rectosigmoidoscopy to determine the distal tumour level), spiral abdominal CT, x ray of the thorax. High resolution MRI of the pelvis is highly recommended for the locoregional staging (cTN) and estimation of the circumferential resection margin (cCRM) in all tumours ≥ cT2. Endorectal ultrasound is mandatory in superficial cancer (≤ cT1N0) when local excision is considered.

Clinical staging and the lower limit of the tumour have a significant impact on the therapeutic strategy to be followed in resectable rectal cancer (Fig. 1).

Adequate TME surgery is sufficient in cStage I tumours (cT1-2N0M0) only. These patients should not undergo neoadjuvant therapy. In contrast, all other patients deserve neoadjuvant treatment. Moreover, the preoperative cTN staging also affects the indication/recommendation for postoperative adjuvant treatment in patients who underwent neoadjuvant radiochemotherapy for tumour downsizing or downstaging (with complete response, i.e. no tumour found, in about 20% of them). Thus, pre-treatment differentiation between cT2 and cT3, between cN0 and cN+, and determination of the cCRM and of some other features of poor prognosis are crucial for preoperative (Fig. 1) and postoperative decision making.

Besides cTN and cCRM determination, high-resolution MRI is able to identify some poor prognostic

tumour features: extramural spread > 5 mm, nodal involvement, extramural venous invasion, and peritoneal infiltration (9). Determination of the cCRM proved to be an appropriate method to predict the curative character of TME surgery, i.e. resection with a pathological tumour-free margin of 1 mm or more. Any resection short of this results in an increased local recurrence rate and decreased survival. Even a tumour-free lateral margin of > 1 mm but < 2 mm at pathological examination was found to be related to an increased local recurrence rate (10, 11). TME with or without a short regimen of preoperative radiotherapy is unable to achieve a R0 if the cCRM is small. In the Dutch TME trial, 23% of the circumferential margins were microscopically positive in the global series. Risk factors for local recurrence after TME surgery were identified: tumour at ≤ 10 cm above the anal verge, stage II-III tumours (3). This indicates that a preoperative long schedule of radiochemotherapy might be of benefit in these patients. At MRI as well as at pathological examination, the distance between the deepest point of invasion to the nearest circumferential surface (mesorectal fascia) should be measured and reported in mm. No distinction should be made between the various modes of invasion i.e. direct spread, involved lymph node, lymphatic or vascular spread. A histological tumour-free margin of at least 1 mm can be predicted with high confidence when the measured distance on preoperative high-resolution MRI is at least 5 mm (12). Alternatively, a cCRM of 1 mm or less has been used as a criterion to predict resection margin involvement (13). Preliminary results of the Mercury Study indicate the feasibility and reproducibility of high-resolution MRI in several European centres as well as the equivalence of MRI with histopathology to predict the CRM status (14).

Metastatic disease

About 20-25% of patients with rectal cancer have metastatic disease (cStage IV) at presentation. If fit for therapy of the primary tumour and its metastases, they should be accurately staged with thoraco-abdominal spiral CT scan and whole body PET scan.

Patients with resectable metastatic disease in the liver and/or lung, are considered for neoadjuvant therapy, resection of the primary and its metastases in one or two sessions, and postoperative chemotherapy.

Patients with unresectable metastatic disease are considered for combination chemotherapy, preferentially in the context of a clinical trial. Since the introduction of combination regimens, the median survival has increased from 10 to 20 months (15).

Imaging, including PET scan, plays an important role not only in the pre-treatment evaluation of these patients, but also in the evaluation of the therapeutic response, in the documentation of resectability after chemotherapy, and in the determination of the progression-free survival.

Imaging during follow-up

There is evidence that intensive follow-up for the detection of recurrent disease improves survival. The local recurrence rate is low (< 10%) after TME surgery and preoperative radio(chemo)therapy. However, the observed survival after 'curative' treatment of Stage I-III rectal cancer still is 58-76% at 5 years (2, 5, 7). Thus, metastatic disease remains a challenge. Patients that are at risk and fit should be offered thoracic and abdominal/liver imaging every 3-6 months during the first three postoperative years with the purpose of detecting operable liver and/or lung metastases. Typically, a chest x-ray and liver US are performed. Very recently, the ASCO (American Society of Clinical Oncology) guidelines recommend annual CT of the thorax and abdomen for 3 years after primary therapy for stage II or III cancer patients (16). In case of recurrent disease that might be amenable to surgery or in case of increasing CEA levels without evident lesion(s) on routine imaging, a PET/CT scan may be indicated.

Conclusion

It is the aim that all teams involved in the treatment of patients with rectal cancer in Belgium will participate in PROCARE. The following factors should motivate individual physicians and teams: the multidisciplinary, national and decentralised character of the project, the fact that professionals are organising and running the project, the anonymous character of the central database, scientific and governmental support, regular information and feedback.

After the audit of instructors and decentralised instruction of all teams willing to participate, a national multidisciplinary campaign will be launched in 2007.

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For further information concerning the Procare project, particularly standardized MRI exams, staging processes as well as reporting, see http://www.rbrs.org
(note from the Editor)