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Simple criteria to predict margin involvement after chemoradiotherapy and sphincter-sparing for low rectal cancer☆

F. Dumont [a,*], C. Tilly [a], P. Dartigues [b], D. Goéré [a], C. Honoré [a], D. Elias [a]

[a] *Department of Digestive Oncological Surgery, Gustave Roussy Cancer Campus, Villejuif, France*
[b] *Department of Histopathology, Gustave Roussy Cancer Campus, Villejuif, France*

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Abstract

Background: Low rectal cancers carry a high risk of circumferential margin involvement (CRM+). The anatomy of the lower part of the rectum and a long course of chemoradiotherapy (CRT) limit the accuracy of imaging to predict the CRM+. Additional criteria are required.
Methods: Eighty six patients undergoing rectal resection with a sphincter-sparing procedure after CRT for low rectal cancer between 2000 and 2013 were retrospectively reviewed. Risk factors of CRM+ and the cut-off number of risk factors required to accurately predict the CRM+ were analyzed.
Results: The CRM+ rate was 9.3% and in the multivariate analysis, the significant risk factors were a tumor size exceeding 3 cm, poor response to CRT and a fixed tumor. The best cut-off to predict CRM+ was the presence of 2 risk factors. Patients with 0–1 and 2–3 risk factors had a CRM+ respectively in 1.3% and 50% of cases and a 3-year recurrence rate of 7% and 35% after a median follow-up of 50 months.
Conclusions: Poor response, a residual tumor greater than 3 cm and a fixed tumor are predictive of CRM+. Sphincter sparing is an oncological safety procedure for patients with 0–1 criteria but not for patients with 2–3 criteria.

Keyswords: Circumferential margin; Low rectum; Rectal cancer; Chemoradiotherapy; Sphincter sparing; Poor response

Introduction

The prognosis of locally advanced rectal cancer has been improved during the last decade due to the combination of long-course neoadjuvant chemoradiotherapy (CRT) and a total mesorectal excision (TME). To date, the local recurrence rate has decreased from 30% to 8%.[1–3]

A positive circumferential resection margin (CRM+) is strongly associated with local and metastatic recurrence despite CRT and TME.[4] A tumor-free margin is also the primary goal of surgery.

In the lower third of the rectum, the CRM has three important specificities.

First, anatomically, the mesorectum becomes narrowed and tapered. The low rectum becomes a bare muscle tube exclusively surrounded by the anal sphincter. At this level, a tumor is always close to the sphincter and the plane of surgery in a sphincter sparing procedure results in a thin CRM. In comparison with upper and mid-rectal cancer, low rectal tumors also have more CRM+.[4,5]

Second, the functional consequences are important because a large margin requires an anal sphincter resection with a permanent stoma. Indeed, there are only two main approaches for low rectal resection, the sphincter-sparing procedure including an intersphincteric resection (ISR) or

☆ Synopsis: This article present simple criteria to predict the circumferential margin involvement after chemoradiotherapy and sphincter sparing for low rectal cancer.

* Corresponding author. Department of Oncological Surgery, 39, Camille Desmoulins, 94805 Villejuif, Cedex, France. Tel.: +33 (0)1 42 11 42 11; fax: +33 (0)1 42 11 53 30.
E-mail address: Frederic.DUMONT@gustaveroussy.fr (F. Dumont).

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the abdominoperineal resection (APR) with a permanent stoma.

Third, the performance of imaging for restaging after a long course of CRT remains challenging[6] in the case of the low rectum.[7] With magnetic resonance imaging (MRI), the signal intensity of the tumor and the anal sphincter is similar. In contrast, the signal intensity of the tumor and mesorectal fat, present in the mid- and upper rectum, is clearly distinct. Moreover, CRT induces changes such as fibrosis and necrosis in normal tissue and the tumor. Imaging fails to differentiate fibrotic spiculation from a residual tumor. The accurate prediction of free margins is more frequently hampered in the case of the low rectum than in that of the upper or mid-rectum.[7]

A fixed tumor, an advanced stage and poor response to CRT have been reported to be factors indicating a higher rate of CRM+.[8–10] However, the influence of these factors has not been established for the specific high-risk group of low rectal cancers treated with irradiation and sphincter-preserving surgery.

This study aims to assess relevant and simple factors influencing CRM+ and to help surgeons choose between a sphincter-sparing procedure (with a thin surgical margin) and the APR (with a larger surgical margin).

Patients and methods

Patients

All consecutive patients who had undergone sphincter-sparing rectal resection for low rectal cancer between January 2000 and December 2013 at our tertiary referral cancer center were retrospectively analyzed. Inclusion criteria were a TME with sphincter sparing after a long course of CRT for a low rectal adenocarcinoma defined as a tumor-anal ring distance of less than 3 cm.

Preoperative staging included a clinical examination, colonoscopy, endorectal ultrasonography (EUS) and/or MRI for primary tumor and nodal staging and a CT scan of the lung, abdomen and pelvis for staging of metastasis.

Pretherapeutic staging included a clinical examination, carcinoembryonic antigen (CEA) determination, a computed tomography (CT) scan, MRI and/or EUS. MRI, used to assess response to CRT, had been performed regularly since 2011 and was not analyzed in this study. The clinical parameters (tumor fixity, annularity and location) were assessed after CRT and just before surgery.

Histopathology

The specimens were pinned under tension onto a wooden board and examined fresh to measure the tumor size and to determine the macroscopic and microscopic distal and lateral margin. The circumferential margin was defined as the minimal distance between the tumor and resection margin. Circumferential or distal resection margins were considered positive when cancer cells were present within 1 mm of the margin. Tumors with acellular mucin pools in the whole specimen were classified as a complete response. The 10th UICC staging system had been used to classify the primary tumor and tumor regression grading (TRG). The TRG definition was: TRG0: no viable cancer cells, TRG1 single cells or small groups of cancer cells, TRG2 residual cancer outgrown by fibrosis, TRG3 minimal or no tumor eradication. Pathology reports and/or the histologic analysis were reviewed by one pathologist (P.D.) to standardize the results. A tumor response was defined as good for TRG 0 or 1 and poor for TRG 2 and 3.

Treatment

The indications for a sphincter-sparing procedure were a free intersphincteric space and an external sphincter without tumor invasion. This local assessment had been performed by pretherapeutic imaging (MRI or EURS) and a clinical examination.

Protracted radiotherapy was a long course of fractionated radiotherapy (45 Gy) with an additional boost of 5.2 Gy to the tumor in 25 fractions over 5 weeks (180 cGy/fraction; 5 days/week). Concurrent chemotherapy was continuous 5 Fluorouracil and Leucovorin or Capecitabine. All patients had undergone a TME with the objective of avoiding rectal fascia injury. An intersphincteric resection (ISR) had been carried out for very low tumors with internal sphincter involvement or a tumor-dentate line distance of less than 1 cm. The laparoscopy and the assessment of quality of mesorectal excision began in 2009.

Follow-up

Follow-up after resection had been done every 3–4 months over two years and every six months over three years. A physical examination, CEA determination, chest X-ray, abdominal ultrasound or abdomino-pelvic CT scan had been performed.

Statistical analysis

Baseline characteristics are described using medians and percentages. A Chi^2 test was used to determine the risk factors associated with a positive CRM (CRM+). Due to the low number of patients and in order to limit statistical bias and alpha risk inflation, only 10 variables were analyzed in the univariate and multivariate analyses. The CRM + factors strictly selected were the relevant and significant variables in the literature. These factors were the body mass index (BMI),[11] the CEA level, clinical pretherapeutic T (cT) and N (cN) staging,[9] response to CRT,[8] the interval between CRT and surgery,[12] the macroscopic tumor characteristics (fixity, annularity, location, size)[10,13–15] and operative pelvic difficulties. This was followed by a

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