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Changing patterns of recurrent disease in colorectal cancer

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Abstract

Background: Due to changes in staging, (neo)-adjuvant treatment and surgical techniques for colorectal cancer (CRC), it is expected that the recurrence pattern will change as well. This study aims to report the current incidence of, and time to recurrent disease (RD), further the localization(s) and the eligibility for successive curative treatment.
Methods: A consecutive cohort of CRC patients, whom were routinely staged with CT and underwent curative treatment according to the national guidelines, was analyzed ($n = 526$).
Results: After a mean and median FU of 39 months, 20% of all patients and 16% of all AJCC stage 0–III patients had developed RD. The annual incidences were the highest in the first two years but tend to retain in the succeeding years for stage 0–III patients. The majority of RD was confined to one organ (58%) and 28% of these patients were again treated with curative intent.
Conclusions: In follow-up nowadays, less recurrences are found than reported in historical studies but these can more often be treated with curative intent. A main cause for the decreased incidence of RD, next to improvements in treatment, is probably stage shift elicited by pre-operative staging. The outcomes support continuation of follow-up in colorectal cancer.

MeSH keywords: Colorectal neoplasms; Recurrence; Neoplasm staging; Follow-up studies

Introduction

In the last decades, several developments in the treatment of colorectal cancer (CRC) have led to a survival improvement.[1,2] Optimal staging, routine use of total mesocolon and mesorectal excision, more extensive surgery and combined treatment modalities are modern approaches towards CRC and its metastases and have resulted in a higher chance on cure.[2–9] These developments can benefit the patient with recurrent disease (RD) as well; a consideration that has contributed to a renewed effort to optimize early detection of RD in follow-up (FU).[10–13]

Due to these changes in staging and treatment, it is expected that the recurrence patterns will also change. Modern staging routines lead to a better division between curable and incurable situations at the onset of diagnosis,[1,14] causing a change in the population that will be in oncological follow-up after treatment (stage shift). (Neo)-adjuvant treatment has led to a decrease in incidence of RD, especially of local recurrences,[7–9,15–17] and may delay recurrences.[18] On the other hand, also more patients with locally advanced or metastatic CRC, whom are at high risk of RD, are nowadays treated with curative intent and will be amongst the FU population. Historical series from the last two decades report a range of RD incidences between 26 and 55%.[19–24] Given these changes it is likely the recurrence patterns are changing as well, but it is

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unclear in what way. In the context of the development of new schedules in oncological follow-up it is important to know what the present recurrence patterns look like.

This study aims to analyze the pattern of recurrence in a consecutive cohort of patients with CRC whom were routinely staged before treatment with abdominal CT and chest X-ray or CT, and treated according to the current standards in (neo)-adjuvant treatment.[25] The analysis concerns the incidence of and time to RD, additionally the type of recurrences including localization(s) and the eligibility for curative treatment.

Patient and methods

Study design

This study is an observational cohort study analyzing the recurrence patterns in a consecutive cohort of patients whom were curatively treated for colorectal cancer and eligible for FU. The study was done at the Medical Spectrum Twente, a large community teaching hospital in the eastern part of the Netherlands. It is a regional referral center for liver and lung surgery, but has no facilities for the treatment of peritoneal carcinomatosis (PC). If necessary, patients are transferred to one of the national referral centers for metastases treatment.

Patient data collection and selection

All patients who underwent surgical treatment for CRC in the period 2007–2010 were prospectively registered in a database designed for colorectal surgery, including patient characteristics, staging, neo-adjuvant treatment, surgical procedure, post-operative course, pTNM stage, adjuvant treatment, treatment of metastases and FU. This baseline cohort was routinely staged with abdominal CT and chest X-ray or CT before treatment and treated according to the current Dutch guidelines. Patients were considered eligible for FU when they were treated with curative intent and alive after discharge (Fig. 1). Patients were considered incurable in case of a macroscopically incomplete (R2) resection of the primary tumor, when the patient had no resection of the primary tumor, or when no intended curative treatment of distant metastases was done. These patients were excluded from the analysis. Data on events during the FU period were retrospectively collected till January 2013 from both paper and digital patient files. Patients that did not have any form of follow-up were also excluded from further analysis (Fig. 1).

Patients' staging, treatment and follow-up

Routine pre-operative staging with a CT of chest and abdomen was introduced as a regional guideline in 2007 and preceded similar national guideline recommendations (2008). CT scanning was performed on a 16 and 64 slice scanner (Toshiba Aquillion 16 and 64) after intravenous

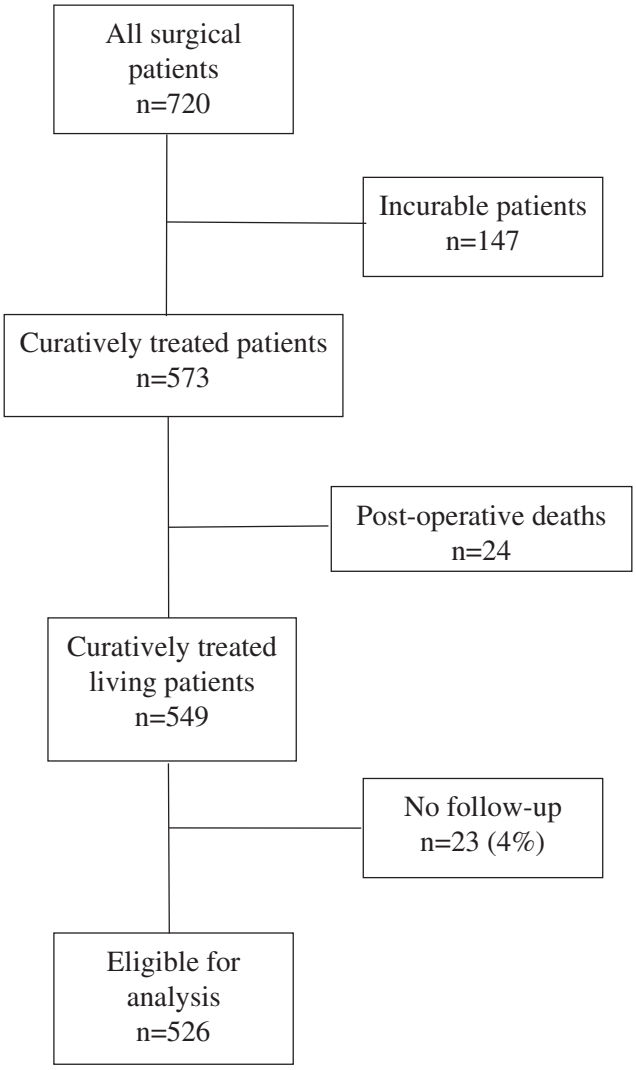

Figure 1. Selection of patient cohort.

contrast injection (visipaque 320, 90 ml, 3 ml/s) in the portal venous phase, with a slice thickness of 1 mm and a reconstruction of 0.8 mm. Patients with rectal cancer up to 12 cm from the anal verge were additionally staged with a pelvic MRI for determination of the local invasion and possible lymph node metastases and received neo-adjuvant (chemo)-radiation in case of a threatened circumferential resection margin and/or the strong suspicion of pathological lymph nodes. Pathological staging was based upon the TNM classification 2002 (6th edition) and classified according to the American Joint Committee on Cancer (AJCC) stages (6th edition), which were the most recent versions at the time of data collection. The diagnosis of synchronous metastases was based upon radiological imaging (CT scan for liver and lung metastases), combined with per-operative findings (for liver and PC).[14,26] For PC histological confirmation was obtained in all cases. Patients with colon cancer with lymph node metastases or unfavorable tumor characteristics such as a pT4 stage, were eligible for adjuvant treatment consisting of 5-FU/Oxaliplatin based