

Is Restaging with Chest and Abdominal CT Scan after Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer Necessary?

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Abstract

Background

There is no evidence regarding restaging of patients with locally advanced rectal cancer after a long course of neoadjuvant radiotherapy with or without chemotherapy. This study evaluated the value of restaging with chest and abdominal computed tomographic (CT) scan after radiotherapy.

Methods

Between January 2000 and December 2010, all newly diagnosed patients in our tertiary referral hospital, who underwent a long course of radiotherapy for locally advanced rectal cancer, were analyzed. Patients were only included if they had chest and abdominal imaging before and after radiotherapy treatment.

Results

A total of 153 patients who met the inclusion criteria and were treated with curative intent were included. A change in treatment strategy due to new findings on the CT scan after radiotherapy was observed in 18 (12 %) of 153 patients. Twelve patients (8 %) were spared rectal surgery due to progressive metastatic disease.

Conclusions

Restaging with a chest and abdominal CT scan after radiotherapy for locally advanced rectal cancer is advisable because additional findings may alter the treatment strategy.

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in men and the second in women.¹ At the time of diagnosis, approximately 25 % of patients already have liver metastases.^{2,3} The lungs represent the second most common site of metastases from colorectal cancer. According to non-population-based studies, lung metastases are present in 10–15 % of patients with colorectal cancer.^{4,5} A population-based study reported that lung metastases are present in 2 % of patients with colorectal cancer.⁶

Distant metastases have implications on the treatment options. For the screening of liver metastases, the Dutch Association of Comprehensive Cancer Centres (ACCC), the National Institute for Health and Clinical Excellence (NICE), and The American Society of Colon and Rectal Surgeons (ASCRS) recommend a computed tomographic (CT) scan or magnetic resonance imaging (MRI). For the screening of lung metastases, they recommend the use of a chest X-ray or a chest CT scan.⁷⁻⁹

Locally advanced rectal cancer has a higher risk of developing lung metastases than colon cancer.^{6,8,10} In patients with locally advanced rectal cancer, improved local control can be achieved with a long course of preoperative radiotherapy in combination with low-dose neoadjuvant chemotherapy as a radiosensitizer.¹¹ However, no advice is provided by ACCC, NICE, or ASCRS in any guideline regarding restaging of patients after neoadjuvant treatment of locally advanced rectal cancer—that is, repeating the imaging, after a long course of neoadjuvant radiotherapy treatment, to ensure that in the intervening time no metastases have developed. This study evaluated the value of restaging patients with locally advanced rectal cancer with a CT scan.

Patients and Methods

Between January 2000 and December 2010, data from all newly diagnosed patients who received a long course of radiotherapy for locally advanced rectal cancer in our tertiary referral hospital were analyzed. Patients were included if they had a chest and abdominal CT scan before and after radiotherapy treatment. An MRI was used for local staging before and after radiotherapy. Neoadjuvant treatment was provided with curative intent. Patient characteristics were collected retrospectively. The database comprised data on age, gender, radiation time and dose, simultaneous chemotherapy, pre- and postradiotherapy chest and abdominal CT scan, pathological primary tumor stage, lymph node stage, and type of surgery.

CT Scan

All CT scans were assessed by radiologists in regular clinical practice. Whenever there was any doubt concerning lesions found on the CT scans, then these scans were reassessed by a panel of radiologists and discussed in a multidisciplinary meeting.

Images were acquired after intravenous injection of 150 mL contrast material at 3.5 mL/s with a delay of 80 s. In addition, an arterial phase scan of the liver was acquired at a delay of 30 s. Positron emission tomography scan is not used as standard protocol in our center.

Locally Advanced Rectal Cancer

Locally advanced rectal cancer was defined in our center as a histological proven adenocarcinoma with one of the following characteristics: tumor >5 cm at colonoscopy and MRI (clinically large T3); clinically fixed tumor or with ingrowth in adjacent organ on MRI (T4); N+ tumor (lymph node >8 mm and/or >4 nodes >5 mm on CT scan or MRI). T4 tumors, but also advanced T3 tumors with a close relation to the circumferential margin, were considered as locally advanced rectal cancer. Regardless of size criteria, any lymph node depicted on MRI with an irregular border or mixed signal intensity was considered suspicious for metastasis.

All patients with locally advanced rectal cancer were discussed in a multidisciplinary team that consisted of colorectal surgeons, hepatobiliary surgeons, gastroenterologists, surgical oncologists, medical oncologists, radiation oncologists, radiologists, pathologists, and nurse practitioners.

Chemoradiotherapy

In our center, patients with locally advanced rectal cancer have been treated with a long course of neoadjuvant radiotherapy: 45–50 Gy (in fractions of 1.8–2 Gy) with or without chemotherapy (capecitabine 825 mg/m² twice a day only on radiotherapy days).¹² We selected patients who did not receive chemotherapy as a result of their comorbidities. Radiotherapy was followed by surgery with a delay of 6–10 weeks. Intraoperative radiotherapy was applied if the circumferential margin was <2 mm.¹³ No laparoscopic resections were performed.

Statistical Analysis

Descriptive statistics are expressed as median (interquartile range [IQR]). Pre- and post-CT variables are expressed as binary variables and compared with the McNemar test for paired data. If fewer than 25 cases change values from the first variable to the second variable, the binomial distribution is used to compute the probability. The SPSS statistical software package (version 17.0; SPSS, Chicago, IL) was used for statistical analysis, where a *P*-value of ≤0.05 was considered statistically significant.

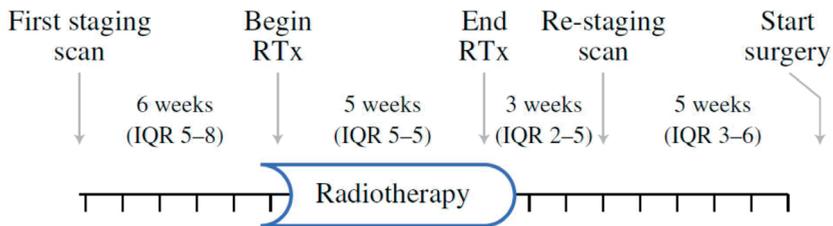
Results

Between January 2000 and December 2010 over 2000 patients were treated with neoadjuvant radiotherapy for rectal cancer. Patients were excluded for receiving radiotherapy for recurrence, palliative radiotherapy, primary radiotherapy treatment, postoperative radiotherapy treatment, and liver-first treatment¹⁴; and for not have imaging studies available.

A total of 153 patients with primary locally advanced rectal cancer had imaging studies available before and after radiotherapy treatment. A chest CT scan before radiotherapy treatment was not performed in 36 patients; they received a chest X-ray. All other patients had an abdominal and chest CT scan. The majority of patients were men (61 %), and the median age was 62 (IQR 53–69.5) years. All 153 patients had a chest and abdominal CT scan after radiotherapy.

The median time between the staging scan and the start of radiotherapy was 6 weeks (IQR 5–8). The time between end of radiotherapy and the postradiotherapy staging scan was 3 weeks (IQR 2–5). The median time between the two scans was 15 weeks (IQR 12.5–17). The median time between the end of radiotherapy and surgery was 9 weeks (IQR 8–10). The median time between the postradiotherapy scan and surgery was 5 weeks (IQR 3–6) (*Fig. 1*).

Figure I. Time interval of treatment



Chest and abdominal CT scans after radiotherapy demonstrated significant additional findings of metastases compared to the scans before radiotherapy, 11 patients (five liver metastases, five lung metastases, and one with both liver and lung metastases) versus 25 patients (14 liver metastases, seven lung metastases, and four with both liver and lung metastases) ($P = 0.001$). Details of the CT scan findings before and after radiotherapy are described in *Table I*.

Table I: Diagnostic findings of restaging after radiotherapy

Before RTx	After RTx	No. of patients
Normal	Normal	96
Normal	LrM	6
Normal	LrM + lung IL	1
Normal	LrM + lung LNS	1
Normal	LrM + LnM	1
Normal	LnM	3
Normal	Liver IL	6
Normal	Lung IL	5
Normal	Lung LNS	3
Liver IL	Normal	5
Liver IL	Liver IL	1
Liver IL	LrM	2
Liver LNS	Normal	1
Liver LNS	Liver LNS	2
LrM	LrM	2
LrM	LrM + LnM	2
LrM	LrM + lung LNS	1
LrM + LnM	LrM + LnM	1
Lung IL	LrM	1
Lung IL	Lung IL	1
Lung IL	Lung LNS	2
Lung IL	Normal	3
LnM	Normal	1
LnM	LnM	4
Liver IL + lung IL	Lung LNS	1
Liver LNS + lung LNS	Liver LNS + lung LNS	1

RTx radiotherapy, LrM liver metastases, LnM lung metastases, IL indeterminate lesions, LNS lesions not suspicious

Of the 153 patients treated with neoadjuvant radiotherapy with curative intent, 107 received a long course of chemoradiotherapy and 46 a long course of radiotherapy only. In ten patients, metastases were detected on the staging scan before radiotherapy, and in 143 patients, the scan before radiotherapy did not reveal any metastases. Of the 143 patients without metastases on the staging scan before radiotherapy, 15 patients (10 %) had metastases on the restaging scan after radiotherapy. A change in treatment strategy due to new findings was carried out in 13 patients (9 %). A resection for rectum carcinoma was not performed in 7 (5 %) of 143 patients (Table II).

Table II. Metastases found on restaging scan in 143 patients with previously undetected metastases

Before RTx	RTx	After RTx	Treatment	Change in treatment strategy
Normal	RTx	LrM + lung IL	Palliative CTx	Yes
Normal	CTx, RTx	LrM + LnM	Palliative CTx	Yes
Normal	CTx, RTx	LrM	LAR + liver resection	Yes
Normal	CTx, RTx	LrM	LAR + liver resection	Yes
Normal	CTx, RTx	LrM	Palliative CTx	Yes
Normal	CTx, RTx	LrM	LAR + liver resection	Yes
Normal	RTx	LrM	Palliative CTx	Yes
Normal	CTx, RTx	LrM + lung LNS	LAR + liver resection	Yes
Normal	RTx	LrM	Palliative CTx	Yes
Normal	CTx, RTx	LnM	APR + SRx	Yes
Normal	CTx, RTx	LnM	APR (palliative) + palliative CTx	Yes
Normal	RTx	LnM + other	LAR (palliative)	No
Liver IL	CTx, RTx	LrM	LAR + liver resection	Yes
Liver IL	RTx	LrM + other	Palliative CTx	Yes
Lung IL	CTx, RTx	LrM	Laparotomy, peritoneal carcinomatosis → palliative CTx	No

RTx radiotherapy, CTx chemotherapy, LAR low anterior resection, APR abdominal perineal resection, LrM liver metastases, LnM lung metastases, SRx stereotactic body radiation, IL indeterminate lesions, LNS lesions not suspicious

In the ten patients with metastases detected on the staging scan before radiotherapy, a change in treatment strategy was carried out in 5 (50 %) as a result of new findings on the postradiotherapy staging scan. A resection for rectum carcinoma was not performed in 5 (50 %) of ten patients (Table III).

Table III. Metastases found on restaging scan in 10 patients with previously detected metastases

Before RTx	RTx	After RTx	Treatment	Change in treatment
LrM	RTx	Progression of LrM	Palliative CTx	Yes
LrM	CTx, RTx	LrM	LAR + liver resection	No
LrM	CTx, RTx	LrM	LAR + liver resection	No
LrM	CTx, RTx	LrM + LnM	Palliative CTx	Yes
LrM	RTx	LrM + LnM	Palliative CTx	Yes
LnM	CTx, RTx	LnM	APR	No
LnM	CTx, RTx	LnM	LAR	No
LnM	RTx	Progression of LnM	Supportive care	Yes
LnM	CTx, RTx	LnM	APR + lobectomy	No
LrM + LnM	RTx	LrM + progression of LnM	Palliative CTx	Yes

RTx radiotherapy, CTx chemotherapy, LAR low anterior resection, APR abdominal perineal resection, LrM liver metastases, LnM lung metastases

In the total group of 153 patients, a change in treatment strategy due to new findings was carried out in 18 (12 %). None of the patients had false-positive metastases on pathology and/or follow-up. Twelve (8 %) of 153 patients were spared rectal surgery as a result of new findings.

Discussion

We evaluated the value of restaging with CT scan for distant metastases after neoadjuvant radiotherapy with or without chemotherapy in patients with locally advanced rectal cancer. A change in treatment strategy due to new findings was observed in 12 % of the patients. In the total group, 8 % of patients were spared rectal surgery due to progressive metastatic disease. Local staging of rectum carcinoma has important implications for the choice of optimal treatment. In patients with locally advanced rectum cancer, improved local control can be achieved with a long course of preoperative radiotherapy in combination with neoadjuvant chemotherapy.¹⁵

Distant metastases have implications on the treatment options. For the screening of liver metastases, there is consensus among oncologists that CT or MRI be performed. For the screening of lung metastases, they recommend the use of a chest X-ray or a CT scan.⁷⁻⁹

It is known that locally advanced rectal cancer has a higher risk of developing metastases than colon cancer.^{5,6,8,10} The recommended treatment for locally advanced rectal cancer is a long course of radiotherapy with or without chemotherapy.⁸ Surgery is usually planned 6–10 weeks after finishing neoadjuvant therapy. During these 3 months, metastases can develop that previously were too small to be detected or were not present at all. Therefore, it seems prudent to restage the patient for distant metastases after radiotherapy and before commencing surgery because new findings in this relatively long period might alter the treatment options. In case of unresectable metastatic disease, resection of the primary tumor is unnecessary from an oncological point of view.¹⁶⁻¹⁹ Through restaging, patients might therefore be spared an unnecessary extensive pelvic operation.

We found a large interval between the staging scan and the beginning of radiotherapy. Most patients were referred to our hospital, and this wide interval is a consequence of logistic management. We do not know whether this wide range has an influence on the outcome of our study.

Local staging techniques have previously been described for locally advanced rectal cancer.²⁰⁻²⁵ To our knowledge, this is the first study describing restaging for distant metastases after radiotherapy and before commencing surgery in patients with locally advanced rectal cancer.

Restaging is only necessary if there are consequences for the treatment strategy in case of additional diagnostic findings. Additional findings can result in treatment of metastases, or in case of unresectable metastases, no resection of rectal tumor and optional treatment with palliative chemotherapy. In our series, 12 % of the total group of 153 patients had a change in the treatment due to findings on the postradiotherapy CT scan. A resection for locally advanced rectal cancer was prevented in 67 % of the latter patients as a result of findings on the postradiotherapy CT scan.

Several studies have demonstrated the abdominal CT scan to be a reliable diagnostic tool for detecting liver metastases, and CT scan has proven to be better than ultrasound.²⁶⁻²⁸ There are limited data describing the optimal chest staging strategy for these patients.²⁹ Some authors conclude that the low incidence of pulmonary metastases and minimal consequences for the treatment plan limits the clinical value or routine staging chest CT before operation.^{29,30} It has several disadvantages such as cost, radiation exposure, and prolonged uncertainty due to the frequent finding of indeterminate lesions.³⁰ However, these results were not assessed in the selected group of patients with locally advanced rectal cancer. Choi et al. demonstrated that staging before neoadjuvant radiotherapy with a chest CT for patients with locally advanced rectal cancer seems reasonable.⁴ Moreover, these patients can benefit from resection of pulmonary metastases because resection can significantly improve survival.³¹ In our specific patient population, all patients will have two CT scans at a median interval of 15 weeks. In case of indeterminate lesions, this will help differentiate between metastases and benign lesions.

We recognize the limitations of this retrospective study in our single-center database; patients were not randomized to have a restaging scan or not, with all inherent biases. Only patients who had complete imaging before and after radiotherapy were included. However, more patients received restaging scans but not all preoperative imaging was available. Not including these patients can cause bias in this study.

In conclusion, this study demonstrated that restaging with a CT scan after radiotherapy is a worthwhile step in the treatment of locally advanced rectal cancer because additional findings may alter the treatment strategy.

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