Original research

Routine preoperative restaging CTs after neoadjuvant chemoradiation for locally advanced rectal cancer are low yield: A retrospective case study

Jennifer S. Davids, Karim Alavi, J. Andres Cervera-Servin, Christine S. Choi, Paul R. Sturrock, W. Brian Sweeney, Justin A. Maykel*

University of Massachusetts Medical School, Division of Colon and Rectal Surgery, Department of Surgery, Worcester, MA 01602, USA

HIGHLIGHTS

- The routine practice of restaging CTs for rectal cancer is not supported by data.
- This small retrospective study showed that routine restaging CTs were low yield.
- Larger studies are needed to determine which patients may benefit from restaging CTs.

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ABSTRACT

Introduction: Pre-operative restaging CT scans are often performed routinely following neoadjuvant chemoradiotherapy for locally advanced rectal cancer. There is a paucity of data on the utility of this common practice. We sought to determine how often restaging CTs identified disease progression or regression that altered management. Methods: We performed a single-institution retrospective study. From 2007 to 2011, 182 patients had newly-diagnosed, non-metastatic rectal adenocarcinoma, of which 96 were surgical candidates with clinical stage II/III disease. Ninety-one of these patients (95%) completed neoadjuvant chemoradiation. Results: Eighty-three out of 91 patients (91%) had restaging CTs. Four patients (5%) had new lesions suspicious for distant metastasis (2 lung, 2 liver) on restaging CT scan reports (1 of these was present on initial staging CT but not reported). All 4 patients had node-positive disease. In no case did restaging CT result in a change in surgical management. Discussion: Because of the financial costs and established risks of intravenous contrast and cumulative radiation exposure, it may be advisable to take a more selective approach to preoperative imaging. Larger, prospective studies may enable identification of an at-risk cohort who would benefit most from restaging CT.

Conclusion: Routine restaging CT scans are low yield in the management of locally advanced rectal cancer.

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1. Introduction

In the United States, over 40,000 new cases of rectal cancer are diagnosed each year [1]. For patients with newly-diagnosed rectal adenocarcinoma, the role of initial staging computed tomography (CT) scans of the chest, abdomen, and pelvis is well-established [2–4]. CT scans are 75–100% sensitive for detection of distant colorectal cancer metastases [5,6]. For local staging of the primary tumor, CT is less sensitive than MRI or endorectal ultrasound; however, it has been shown to have 55–70% accuracy in identifying nodal disease, and 73% accuracy for T staging [7–9]. Twenty percent of patients with rectal cancer will have metastatic disease at the time of presentation [10]. Five-year overall survival for metastatic rectal cancer is only 6%, and only 20–30% of this group is eligible for metastasectomy with curative intent [11–13]. Accurate staging of both local and distant disease is therefore instrumental in providing appropriate care for patients with rectal cancer.

Most patients with locally advanced (clinical stage II–III) mid or low rectal cancer who are surgical candidates receive neoadjuvant...
5-FU-based chemotherapy and pelvic radiation prior to surgical resection [14]. Despite a lack of supportive evidence, it is common practice at many institutions to obtain routine restaging CT scans of the chest, abdomen, and pelvis following completion of neoadjuvant therapy. Restaging CT scans have the potential to impact management by identifying new distant metastases or local disease regression or progression. Detection of new distant metastases may alter management by prompting the use of additional chemotherapy, synchronous or staged metastasectomy, or non-operative/palliative care.

Local disease progression may suggest the need for a more extended resection including en bloc resection of involved pelvic organs or partial sacrectomy, or the tumor may be deemed unresectable. Alternatively, the tumor may regress and more defined tissue planes predict a less extended resection. Several studies have compared the efficacy of various imaging modalities in determining the primary tumor response to neoadjuvant therapy, and the capacity to predict final pathologic staging. The primary limitation, which is common to all imaging modalities, is the inability to distinguish treatment-related fibrosis and edema from tumor [15]; nevertheless, CT has been shown to effectively exclude advanced T stages (ypT4) and circumferential resection margin involvement, with high specificity for N staging [16].

Current National Comprehensive Cancer Network (NCCN) [17] and American Society of Colon and Rectal Surgeons (ASCRS) [18] practice guidelines do not provide recommendations on the appropriateness of restaging CT scans or their role in the routine care of patients with locally advanced rectal cancer. Although restaging CTs are a common practice, minimal literature exists that either supports or refutes the use of these scans. There are no definitive data on the actual diagnostic yield of restaging CT scans in patients receiving neoadjuvant 5-FU based chemotherapy and pelvic irradiation for locally advanced rectal cancer.

CT scans have inherent risks for the patient and increase overall healthcare costs. Contrast-induced nephropathy and allergic reactions to iodinated contrast can be observed in patients undergoing CT imaging [19–21]. Moreover, there is an increasing awareness about the negative consequences of cumulative radiation exposure, such as an increased risk of malignancy [22]. In addition, nonspecific findings on CT scans often compel clinicians to pursue additional, more costly work-up. In the era of bundled payments, streamlining patient care by minimizing low-yield diagnostic studies has never been more important.

The primary aim of this study was to determine how frequently findings on routine restaging CT scans altered surgical management. We hypothesized that routine restaging CT scan following the completion of neoadjuvant chemoradiation did not change the treatment of rectal cancer with regard to the surgical plan.

2. Methods

Approval to initiate the study was obtained from our Institutional Review Board. The UMass-Memorial Tumor Registry was queried to identify all patients with newly diagnosed biopsy-proven rectal adenocarcinoma from 2007 through 2011. The Electronic Medical Record (EMR) for each patient was reviewed by an experienced clinician. Demographic data included patient age and gender. Clinical data included preoperative clinical stage; endorectal ultrasound, MRI, and CT scan reports; initial carcinoembryonic antigen (CEA) level; type and duration of chemoradiotherapy; type of resection performed; surgeon specialty (colon and rectal surgeon, surgical oncologist, or general surgeon); intraoperative findings; final pathologic stage; length of postoperative follow-up; local and distant disease recurrence; and mortality. Data were obtained from office and inpatient consult notes, operative reports, radiology and pathology reports. Patients were excluded based on the following criteria: metastases at diagnosis, recurrence of previous rectal cancer, not surgical candidates or refusal of surgery, or surgery performed at an outside institution with incomplete data in our EMR.

All patients included in the analysis had staging CT scans of the chest, abdomen, and pelvis performed at the time of diagnosis. A subset of patients also had PET scan at the time of diagnosis. Neoadjuvant treatment consisted of standard concurrent 5-FU based chemoradiation and 50.4 Gy pelvic radiation. “Re-staging” CT scans were performed following documented completion of chemoradiotherapy, prior to surgery. In some cases, restaging PET was also performed. Transanal excision included conventional full-thickness resection as well as Transanal Endoscopic Microsurgery (TEM); low anterior resection (LAR) included both laparoscopic-assisted and open procedures, with and without diverting loop ileostomy. Abdominoperineal resection (APR) included laparoscopic-assisted procedures and conventional open procedures. Final pathologic stage is documented according to American Joint Committee on Cancer (AJCC) 6th edition (pre-2010) and 7th edition (from 2010-on) [23,24].

3. Results

A total of 182 patients were identified with a new diagnosis of nonmetastatic rectal adenocarcinoma (mean age 64, 56% male; Fig. 1). Eighty-six patients were excluded from further review for the following reasons: 61 patients had clinical stage I disease and did not receive neoadjuvant therapy, 10 declined surgery, 9 were not surgical candidates due to medical co-morbidities, and 6 had surgery at other institutions.

Ninety-six patients were surgical candidates with clinical stage II–III disease. Three patients did not receive radiation therapy because they had prior pelvic radiation for prostate cancer, and 1 patient did not receive any neoadjuvant treatment due to thrombocytopenia. Of the 92 remaining patients (mean age 60, 61% male), all completed neoadjuvant chemoradiotherapy except for 1 patient who discontinued chemotherapy early due to toxicity. Of the 91 patients who completed neoadjuvant therapy, 84 (92%) had their resection performed by a board-certified colon and rectal surgeon; 4 (4%) were performed by a general surgeon, and 3 (3%) by a surgical oncologist.

Following completion of neoadjuvant chemoradiotherapy, 83 of the 91 patients (91%) had restaging CT scans of the chest, abdomen, and pelvis. The mean duration between initial staging and restaging CT scans was 106 days (range 76–169 days). There were no documented iatrogenic injuries (such as contrast-induced allergy

![Fig. 1. Patient subsets.](image-url)
or nephropathy) as a direct result of the CT scans. Seven patients had restaging PET scans (all negative for metastasis). Table 1 displays the patient characteristics of restaged and not-restaged patients. The not-restaged group was too small (8 patients) for relevant statistical comparison to the restaged group.

Table 2 shows the breakdown by procedure according to presence or absence of restaging CT scans. Of the 83 restaged patients, 52 had LAR (63%), 28 had APR (34%), and 3 had transanal/TEM resections (3%). Of the 8 patients who were not restaged, 6 had LAR (75%) and 2 had APR (25%). Four restaged patients (5%) were found to have new lesions likely representing metastasis on restaging CT scan reports. The clinical characteristics and outcomes of these patients are summarized in Table 3. Two patients had new lesions suspicious for pulmonary metastases. Two patients had new liver lesions. Of note, one of these patients had an initial staging CT read as negative; a different radiologist (from the same institution) read the restaging scan and noted the presence of a liver lesion, which he recognized was present on the initial scan. According to the report on the restaging CT, the lesion increased in size from 0.8 cm to 1.3 cm. These cases were all discussed in our multidisciplinary GI tumor board, and in all four instances, the decision was made to proceed with the planned surgical resection of the primary tumor. All 4 patients had node-positive disease on final pathology.

Surveillance imaging for the patient with the solitary lung lesion revealed new lung and liver lesions consistent with metastases at 6 months postoperative follow-up, prompting treatment with additional chemotherapy (FOLFIRI regimen) and was then lost to follow-up (care was transferred to a different institution). The patient with new bilateral pulmonary nodules had eventual progression of pulmonary disease 18 months postoperatively, and was started on chemotherapy. The lung lesions were not amenable to resection. She subsequently developed brain metastases and underwent palliative radiation. She died 13 months after surgery. As for the first patient with the liver lesion identified on restaging CT, the lesion was not accessible for simple biopsy or wedge resection during LAR. Postoperatively, the lesion was confirmed to be adenocarcinoma on CT-guided biopsy. The patient was started on FOLFIRI and Avastin, and underwent staged partial hepatectomy 5 months after his rectal cancer resection. He was alive 13 months postoperatively (at last follow-up). The second patient with a liver metastasis identified on restaging CT had multiple liver metastases at laparotomy. The dominant mass was biopsied, confirming metastatic adenocarcinoma. Postoperative surveillance imaging identified new pulmonary metastases. He had multiple co-morbidities and experienced a cerebellar infarct 1 month postoperatively; he was deceased at 4 months postoperatively.

Table 3 shows the clinical characteristics and outcomes of the 4 patients who had new metastases identified on restaging CT scan. *This patient underwent preoperative PET scan and these lesions were not FDG-avid. **Denotes patient for whom the initial staging CT report was negative; restaging CT (read by a different radiologist) reported an interval increase in the size of a 0.8 cm liver lesion to 1.3 cm.
intraoperatively. Of the 8 patients who were not restaged, no new intraoperative metastases were identified (Fig. 2).

Table 4 shows final pathologic stage data for the restaged patients. Thirteen patients had a complete response (16%), 24 stage I (29%), 12 stage II (14%), 30 stage III (36%), and 4 stage IV (5%).

Follow-up, recurrence, and mortality data are shown in Table 5. Overall median followup was 30 months. Local recurrence occurred in one restaged patient at 68 months and was treated with en bloc resection; she is alive at 72 months follow-up. The overall rate of distant metastasis was only 7.6% (7 patients, not including the 4 patients with metastases identified on restaging CT), and all of these were in the restaged group. Mean time to recurrence was 43 months postoperatively. There were 5 deaths in the restaged group (2 of which had new metastases diagnosed on restaging CT) and none observed in the not-restaged group.

Additional chart review was performed to determine whether the characteristics of the 8 patients who were not restaged were different from the 83 patients who were. Two of the 8 patients who were not restaged had resections performed by non-colorectal surgeons, 1 declined restaging scans, 3 had rigid proctoscopy or flexible sigmoidoscopy to re-evaluate the primary, and in 2 cases the reason could not be determined.

4. Discussion

The findings of this study suggest that the routine practice of obtaining restaging CT scans of the chest, abdomen, and pelvis following neoadjuvant therapy for locally advanced rectal cancer is low yield and does not alter surgical management. Only 4 out of 83 (5%) restaging CT scans identified lesions suspicious for distant metastases. In these cases, the surgical plan remained unaltered, although these findings may have impacted decisions regarding adjuvant chemotherapy and subsequent surgical interventions. In no case did restaging CT scans identify local disease progression prompting a change in surgical work-up or management, such as the need for insertion of ureteral stents, en bloc resection of contiguous organs, or determination of unresectability. No new intraoperative metastases were found in the 8 patients who were not restaged.

This study is unique in that it explores the diagnostic yield of routine restaging CT scans following neoadjuvant chemoradiation for rectal cancer in an academic cancer center that routinely performs these scans. In a related study, Ayez et al. concluded that restaging CT scans are a valuable component of the treatment algorithm, having identified treatment-altering findings in 12% of cases [25]. There are several important differences between these two studies. Over a 10-year period, Ayez et al. identified over 2000 patients who underwent treatment with neoadjuvant radiotherapy (with or without chemotherapy) for locally advanced rectal cancer. Of these patients, only 143 patients underwent restaging CT scans, suggesting the possibility of significant selection bias. Patients sent for restaging scans may inherently have been at higher risk for disease progression. Additionally, of the 143 restaged patients in their study, 46 patients (42%) received radiotherapy only (no chemotherapy). This may account for the high number of patients (11%) with new metastases on restaging CT thus altering treatment strategy in 13 of 15 patients (87%). This finding contrasts with the lower rate of disease progression (4 of 83 patients or 5%) demonstrated in our study and with no subsequent changes in surgical management.

A more recent study by Jaffe et al. found similar results to our study. In a cohort of 88 patients with localized rectal cancer, restaging CT scan did not identify any new metastases [26]. This study did not provide data on initial staging modalities, patient characteristics, follow-up, and rate of recurrence, nor did it assess for local disease progression. Additionally, only 88 of 200 patients (44%) had restaging CT scans performed, again introducing the possibility of selection bias.

Our single institution, retrospective study is limited by a small sample size that renders it underpowered to reveal more subtle differences in the restaged and not-restaged groups. Data on restaging CT scans were based entirely on radiology reports from our own institution and referring facilities, and the original CT scan images were not re-reviewed by an independent, blinded radiologist. Because three of the restaged patients had transanal excisions, the presence or absence of intraabdominal metastasis could not be determined intraoperatively for these patients.

Further, in this series, we retrospectively report the decisions of our own multidisciplinary group in proceeding directly to surgery in the four patients who had new suspicious lesions identified on restaging CT. As there currently is no consensus on the management of synchronous liver metastases, it is understandable that other institutions have different management practices for such patients (such as simultaneous liver and rectal resection, or a “liver-first” strategy), and that could potentially have led to a different conclusion for this subgroup [27,28]. Nevertheless, this subgroup was small, only 4 out of 83 patients (5%), which suggests that, despite the management decisions made on these patients, the overall practice of routine restaging CT is low yield. Lastly, because patients were selected from 2007 to 2011, more long-term follow-up and survival data are not yet available.

Our study suggests that, following neoadjuvant chemotherapy for locally advanced rectal cancer, routine restaging CT scans are of low diagnostic yield for most patients. These findings suggest that a standardized and streamlined approach to the management of rectal cancer, designed to minimize low yield radiographic imaging, may not only reduce health care costs, but also decrease the risks to patients. While none of our patients experienced an iatrogenic injury directly related to CT scans, these tests are not without risk. CT scans with intravenous contrast are associated with risk of contrast-induced nephropathy, particularly in patients with underlying renal insufficiency [21]. Furthermore, allergic reactions to iodinated contrast occur in roughly 3% of scans and can be life-threatening [29]. The risk of radiation from one additional scan is relatively small, but cancer patients often undergo multiple scans throughout their treatment course, so any unnecessary exposure

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should be minimized. According to NCCN practice guidelines for diagnosis and surveillance of rectal cancer, a 5-year survivor of rectal cancer may have as many as 6 CT scans of the chest, abdomen, and pelvis from the time of diagnosis [17]. With nearly 50% of node-positive cancer patients alive at 10 years, this is a legitimate concern.

Future directions of this work include performing a larger, prospective study, which would allow for additional survival data and cost analysis. Such additional investigation may allow for identification of a high-risk cohort (such as node-positive disease or bulky primary) which may benefit more from restaging, thereby favoring a selective, as opposed to a routine approach. This work ultimately has the potential to impact practice guidelines for rectal cancer, which currently do not address restaging CT scans due to the paucity of data on this topic. In the era of accountable care, it is becoming increasingly important to avoid costly diagnostic studies that are unlikely to affect management. For diseases as complex as rectal cancer, a streamlined approach to treatment will enable multidisciplinary teams to provide optimal care while reducing the overall burden on the healthcare system and risk to patients.

Ethics

The authors obtained permission from their Institutional Review Board.

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Author contribution

Davids-study design, data collection and analysis, writing. Alavi-study design, data analysis. Cervera-Servin-study design, data collection. Choi-study design, data collection. Sturrock-study design, data analysis. Sweeney-study design, data analysis. Maykel-study design, data analysis, writing.

Conflict of interest statement

The authors report no conflicts of interest.

References