How Reliable Is CT Scan in Staging Right Colon Cancer?

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BACKGROUND: The observation of inferior oncologic outcomes after surgery for proximal colon cancers has led to the investigation of alternative treatment strategies, including surgical procedures and neoadjuvant systemic chemotherapy in selected patients.

OBJECTIVE: The purpose of this study was to determine the accuracy of CT staging in proximal colon cancer in detecting unfavorable pathologic features that may aid in the selection of ideal candidates alternative treatment strategies, including extended lymph node dissection and/or neoadjuvant chemotherapy.

DESIGN: This was a retrospective consecutive series.

SETTINGS: Trained abdominal radiologists from 2 centers performed a blinded review of CT scans obtained to locally stage proximal colon cancer according to previously defined prognostic groups, including T1/2, T3/4, N+, and extramural venous invasion. CT findings were compared with histopathologic results as a reference standard. Unfavorable pathologic findings included pT3/4, pN+, or extramural venous invasion.

PATIENTS: Consecutive patients undergoing right colectomy in 2 institutions between 2011 and 2016 were retrospectively reviewed from a prospectively collected database.

MAIN OUTCOME MEASURES: T status, nodal status, and extramural venous invasion status comparing CT with final histologic findings were measured.

RESULTS: Of 150 CT scans reviewed, CT failed to identify primary cancer in 18%. Overall accuracy of CT to identify unfavorable pathologic features was 63% with sensitivity, specificity, positive predictive value, and negative predictive value of 63% (95% CI, 54%–71%), 63% (95% CI, 46%–81%), 87% (95% CI, 80%–94%) and 30% (95% CI, 18%–41%). Only cT3/4 (55% vs 45%; $p = 0.001$) and cN+ (42% vs 58%; $p = 0.02$) were significantly associated with correct identification of unfavorable features at final pathology. CT scans overstaged and understaged cT in 23.7% and 48.3% and cN in 28.7% and 53.0% of cases.

LIMITATIONS: The study was limited by its retrospective design, relatively small sample size, and heterogeneity of CT images performed in different institutions with variable equipment and technical details.

CONCLUSIONS: Accuracy of CT scan for identification of pT3/4, pN+, or extramural venous invasion was insufficient to allow for proper identification of patients at high risk for local recurrence and/or in whom to consider alternative treatment strategies. Locoregional overstaging and understaging resulted in inappropriate treatment strategies in <48%. See **Video Abstract** at http://links.lww.com/DCR/A935.

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Funding/Support: None reported.

Financial Disclosures: None reported.

Poster presentation at the meeting of The American Society of Colon and Rectal Surgeons, Seattle, WA, June 10 to 14, 2017 and at the annual meeting of the Association for Coloproctology of Great Britain and Ireland, Bournemouth, UK, July 3-5, 2017.

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Dis Colon Rectum 2019; 62: 960–964
DOI: 10.1097/DCR.0000000000001387

KEY WORDS: Computed tomography scan; Histologic findings; Neoadjuvant chemotherapy; Pathologic features; Right colon cancer; Staging.

Improvements in preoperative radiologic staging with the widespread use of MRI of rectal cancer has contributed to the proper selection of patients at high risk for the development of local recurrence after radical total mesorectcal excision.[1] Features including T-status subclassification, perirectal nodal metastases, suspicious lateral pelvic nodes, and extramural venous invasion are currently used in clinical practice for the selection of patients with rectal cancer who are ideal candidates for neoadjuvant chemoradiation or upfront total mesorectcal excision.[2–5] In colon cancer, however, locoregional staging is rarely used for decision management purposes, because segmental colectomy (without neoadjuvant therapy) with standard lymph node resection has been performed in the majority of cases.

The observation of inferior oncologic outcomes after surgery for proximal colon cancers has led to the investigation of alternative treatment strategies, including surgical procedures and neoadjuvant systemic chemotherapy delivery.[6] Routine central vessel ligation resulting in extended lymph node resection and total mesocolic excision (anatomic dissection of the mesocolon respecting embryonary fascial planes) and/or neoadjuvant chemotherapy before surgical resection have been suggested to improve oncologic outcomes among selected patients with proximal colon cancer.[7–10] Compared with standard surgical resection of proximal colon cancer, more extensive nodal dissection with central vascular ligation and clearance of lymphatic tissue along the mesenteric vessels (D3 dissection) has been associated with improved oncologic outcomes.[9,11] In addition, the use of neoadjuvant chemotherapy strategies has resulted in better pathologic outcomes (R0 resection rates) and significant tumor downstaging (pN0 disease).[6] However, considering the substantial increase in treatment-related morbidity associated with these strategies (including injuries to superior mesenteric vessels and treatment- and chemotherapy-related toxicity), routine implementation of these 2 methods may lead to overtreatment of a significant proportion of patients.[8,10] In this setting, proper preoperative identification of adverse pathologic features by radiologic imaging, mirroring current practice in rectal cancer, could potentially result in precise selection of patients and candidates for more extensive resections (central vessel ligation and complete mesocolic excision) and/or neoadjuvant chemotherapy.[12,13] This individualized approach to proximal colon cancer could minimize unnecessary treatment-related morbidity and maximize oncologic benefit of these alternative treatment strategies. Although there is some evidence that MRI may be superior to CT scan for such purposes (mainly derived from rectal cancer studies), there are scarce data regarding accuracies for the detection of specific high-risk features in right colon cancers with the most commonly used imaging modality (CT). Therefore, the purpose of this study was to determine the accuracy of preoperative CT staging in detecting specific unfavorable pathologic features that could aid in the identification of high-risk patients for local and systemic recurrence and who could ultimately represent ideal candidates for alternative treatment strategies.

PATIENTS AND METHODS

Consecutive patients undergoing right colectomy in 2 institutions between 2011 and 2016 were retrospectively reviewed from a prospectively collected database after institutional review board approval. In both institutions, preoperative CT scanning is considered the preferred method of locoregional and systemic staging for proximal colon cancers. All of the patients undergoing elective resection for right colon cancer (from the cecum to the hepatic flexure using the *International Classification of Diseases*, 10th revision, diagnostic code C18.9, right colon cancer) were eligible for inclusion provided that there was a preoperative abdominal CT scan available for review. All of the patients without an available preoperative CT scan for review were excluded.

CT findings were compared with the final original pathology reports as the reference standard in regards to T status, N status, and extramural vascular invasion (EMVI) status. Unfavorable pathologic findings included pT3/4, pN+, or pEMVI+.

Imaging Evaluation

Three trained GI radiologists with >5 years of experience as faculty retrospectively performed a blinded review of CT scans from 2 independent institutions. Observers were blinded to surgical and final histopathologic results. However, they were all aware of the primary colon cancer diagnosis. Each CT scan was reviewed by a single radiologist/observer.

Tumors were staged according to TNM classification and were grouped based on the presence or absence of tumor invasion beyond the wall of the colon, T1/T2 versus T3/T4. Lymph node metastases were defined as any visible nodes >1 cm or abnormal clustering of >3 normal-sized lymph nodes.[14] We included only nodal size as criteria to simplify the evaluation of this particular feature, because the ability of CT to detect border irregularity and attenuation differences is limited. The presence of EMVI was considered positive if the peritumoral veins showed nodular enhancement or presence of tumor within large veins.[14]

Pathology Reports

Original pathology reports were used for comparison as the reference standard. T-status classifications were grouped as T1/2 versus T3/4. N status was considered positive if ≥1 lymph node was considered as metastatic. Finally, EMVI status was considered positive when specifically reported as

such. In the absence of a specific report, EMVI status was considered negative. Any unfavorable pathologic feature was considered if ≥1 of the following was present: pT3/4, pN+, or pEMVI+. Pathologic examination procedures in both institutions were performed according to standard protocols for colon cancer without any specific fat-clearing solutions for nodal harvest or immunohistochemistry for unfavorable pathologic feature identification. Both institutions have specialized GI pathologists with >10 years of specialized experience. Overall, 3 GI pathologists reviewed all of the cases in each institution.

Statistical Analysis

Descriptive statistics with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were used to assess T status, N status, and EMVI status comparing CT with final histologic findings (XLSTAT Statistical Data Analysis Solutions, Long Island, NY USA).

RESULTS

A total of 150 patients were included (79 men and 71 women), with a median age of 70.2 years (range, 39.0–94.0 y). Briefly, 80.0% of patients had ≥1 unfavorable pathologic result based on the pathology reports: 112 (74.6%) were pT3/4, 69 (46.0%) were pN+, and 28 (18.7%) were pEMVI+. There were no significant differences in pathologic assessment between the institutions. The rates of patients with <12 lymph nodes harvested were 4% and 10% ($p = 0.14$), and the total numbers of patients with pN+ were 44% and 50% ($p = 0.48$). Demographics, clinical, and histologic results of the study population are described in Table 1.

TABLE 1. Demographics and clinical and histologic results of the study population

Variable	*Data (N = 150)*
Age, median (range), y	70.2 (39.0–94.0)
Sex (men:women), n (%)	79 (52.7):71 (47.3)
Clinical stage, n (%)	
cT0	27 (18.0)
cT1/2	49 (32.7)
cT3/4	74 (49.3)
cN (+/–)	56 (37.3)/94 (62.7)
cEMVI. (+/–)	13 (8.7)/137 (91.3)
Pathologic stage, n (%)	
pT0	1 (0.7)
pT1/2	37 (24.7)
pT3/4	112 (74.6)
pN (+/–)	69 (46.0)/81 (54.0)
pEMVI (+/–)	28 (18.7)/122 (81.3)

EMVI = extramural indeterminate invasion.

TABLE 2. Accuracy of CT staging in predicting tumor stage compared with histopathologic results

	Pathologic T stage			
CT T stage	*pT0*	*pT1–2*	*pT3–4*	*Total*
cT0	–	9	18	27
cT1/2	1	19	29	49
cT3/4	–	9	65	74
Total	1	37	112	150

T-Status Accuracy

CT failed to identify the primary cancer in 18% of patients. Sensitivity, specificity, PPV, and NPV for preoperative CT to detect pT1/2 tumors were 50% (95% CI, 34%–66%), 74% (95% CI, 66%–82%), 40% (95% CI, 26%–53%), and 81% (95% CI, 74%–89%) and for pT3/4 tumors were 57% (95% CI, 48%–66%), 76% (95% CI, 63%–90%), 88% (95% CI, 80%–95%), and 38% (95% CI, 27%–48%). CT overstaged and understaged T status in 23.7% and 48.3% of the cases. Overall accuracy was 62% for advanced tumors (pT3/4) and 68% for early tumors (pT1/2). The median tumor size for tumors that could not be identified by CT scan was 4.0 ± 2.1 cm. Final pathologic T stages for nonidentified tumors during radiology were pT1/2 in 9 patients and pT3/4 in 18 patients (Table 2).

Nodal Status Accuracy

Sensitivity, specificity, PPV, and NPV to predict nodal status were 47% (95% CI, 35%–59%), 71% (95% CI, 61%–81%), 59% (95% CI, 46%–72%), and 61% (95% CI, 51%–71%). CT scans overstaged and understaged cN in 28.7% and 53.0% of cases. Overall accuracy was 60% (Table 3).

Extramural Venous Invasion Accuracy

Sensitivity, specificity, PPV, and NPV for detecting EMVI were 8% (95% CI, 3%–19%), 91% (95% CI, 86%–96%), 15% (95% CI, 4%–35%), and 83% (95% CI, 77%–89%). Overall accuracy was 77% (Table 3).

Unfavorable Pathologic Features

Overall accuracy of CT to identify any unfavorable pathologic feature (pT3/4, pN+, or pEMVI+) was 63%. Sensitivity, specificity, PPV, and NPV were 63% (95% CI, 54%–71%), 63% (95% CI, 46%–81%), 87% (95% CI, 80%–94%), and 30% (95% CI, 18%–41%). There were no

TABLE 3. Summary of results of CT staging

Stage	*Sensitivity, %*	*Specificity, %*	*Accuracy, %*
T1/2	50	74	68
T3/4	57	76	62
N	47	71	60
EMVI	8	91	77

EMVI = extramural venous invasion.

differences in accuracy rates for the detection of any unfavorable pathologic feature among the different observers (58%, 60%, and 75%; $p = 0.19$). In addition, there were no differences in accuracy rates over time when comparing the first (2011–2013) and the last 3 years studied (2014–2016; 62.1% vs 65.6%; $p = 0.73$). CT scans were more likely to correctly identify patients with any unfavorable feature among patients with cT3/T4 (55% vs 45%; $p = 0.001$) or cN+ (58% vs 42%; $p = 0.02$).

DISCUSSION

Preoperative staging of right colon cancers with the use of abdominal CT scan is associated with a relatively low accuracy for the identification of patients with high-risk features for local and systemic recurrence. The present study demonstrates that CT scan is able to accurately detect any unfavorable pathologic feature detected in the final histology in less than two thirds of all patients (63%) with proximal colon cancer. Individual selection of specific surgical management of these patients based on preoperative staging using CT scan is probably insufficient.

The depths of tumor penetration through the bowel wall, nodal metastases, and extramural venous invasion are well-recognized prognostic features. Tumors invading through the bowel wall (T3/T4) are more likely to develop local and distant (including peritoneal) relapse. Preoperative identification of such patients could help stratify more aggressive surgical treatment, including more extensive nodal dissection or even prophylactic hyperthermic intraperitoneal chemotherapy (for pT4a colon cancers).[15]

However, in the present study, radiologic identification of primary tumor depth of invasion through the bowel wall showed low accuracy for both early (68%) and advanced tumors (62%) with preoperative CT scan. In addition, in 27 cases (18%) the radiologist could not identify the exact location of the primary tumor. In a recent published meta-analysis including almost 900 patients preoperatively staged for colon cancer,[16] the summary estimates for the detection of T3/4 tumors showed a higher sensitivity of 90% (95% CI, 83%–95%) but a lower specificity of 69% (95% CI, 62%–75%) compared with our results (57% and 76%). The Fluoropyrimidine, Oxaliplatin and Targeted Receptor Pre-Operative Therapy (FOXTROT) trial[6] randomly assigned patients with high-risk colon cancer (preoperative staging by CT scan) to neoadjuvant chemotherapy or surgery alone. Sensitivity and specificity in predicting tumor stage (T3/4 vs T1/2) were 95% (95% CI, 87%–98%) and 50% (95% CI, 22%–77%). Both studies included patients with proximal and distal colon cancers. Inclusion of distal tumors may have accounted for some of the discrepancies between these 2 studies and our findings.

The idea that CT scan is insufficiently accurate to stage proximal colon cancers led Rollvén et al[17] to compare MRI with CT scan for staging 29 patients with colon cancer. MRI resulted in more accurate identification of locally advanced colon cancer defined as tumor stages T3c, d (extramural tumor extensions outside the muscularis propria >5 mm) and T4 (90% vs 79%). In addition, MRI showed increased interobserver agreement in terms of T status ($\kappa = 0.79$ vs 0.64) when compared with CT scan.

In a recent retrospective study by Nerad et al,[18] the use of diagnostic MRI was studied in the setting of local staging for colon cancer. Images were retrospectively analyzed by 2 blinded independent readers and compared with histopathology as the reference standard. Sensitivity (91%) and specificity (84%) for detecting T3/4 disease were considerably higher than our results with the use of CT scan. These differences were at least partially attributed to the superior soft-tissue contrast of MRI when compared with CT scan, allowing for more accurate detection of serosal involvement.

Detection of nodal involvement resulted in even worse outcomes. Our results showed a very low sensitivity of 47% and specificity of 71%, similar to previously reported data.[12,16,17] Dighe et al[12] suggested that the use of the CT to identify high-risk tumors based on N status would be inappropriate, describing an accuracy of 55%. Studies comparing MRI and CT scan showed no significant differences in nodal status accuracy.[15] Curiously, false-negative CT scans were observed in 25% of our series. Therefore, performance of extended nodal dissection with central venous ligation and D3 lymphadenectomy exclusively to radiologic cN+ would have failed to provide appropriate treatment to a significant proportion of patients. Conversely, the relatively low false-positive rates (15.3%) indicate that very few patients would have undergone potentially unnecessary extensive surgery.

Our results showed a very low sensitivity of 8% for the detection of EMVI but a high specificity of 91%. A lack of sufficient expertise in radiologic EMVI identification through CT imaging and the absence of standardized pathologic reporting of this particular finding may have contributed to these results. Similar findings have been reported by the FOXTROT trial,[12] with a sensitivity of 47% and a specificity of 68% to identify EMVI. In contrast, MRI may be superior to CT, specifically for the detection of EMVI. The comparison of MRI and CT scan for this particular feature resulted in higher sensitivity with MRI (75% vs 37%). One study even described a sensitivity of 100% for the preoperative radiologic identification of EMVI by MRI.

Several limitations of our study may warrant additional investigation. First, the retrospective design and the relatively small sample size may have accounted for some of the observed results. Still, it remains one of the larg-

est series correlating radiologic and specific pathologic high-risk features exclusively for proximal colon cancer. Second, the heterogeneity of the technique used for acquisition of CT images performed in different institutions with the use of variable equipment and different technical details and preparations may have accounted for a significant source of bias in our study. Conversely, these results may reflect real-world outcomes and increase the applicability of our findings to current clinical practice. Unfortunately, CT scans were reviewed by a single radiologist, which prevented proper interobserver agreement estimates, which is a significant limitation of this study. Finally, it remains unclear whether more accurate radiologic staging of these specific unfavorable features will translate into clinically relevant outcomes that may be influenced by surgical management changes. In fact, the outcomes of more extensive surgery recently reported with central venous ligation and D3 dissection for colon cancers has suggested an oncologic benefit to all pathologic stages, including early T stage and node-negative disease (not only for high-risk colon cancers). Therefore, it remains to be demonstrated whether more accurate staging will lead to more individualized treatment with actual improvements in outcomes while minimizing the risk of unnecessary morbidity.[9,19]

CONCLUSION

The accuracy of CT scan for the identification of any high-risk feature in proximal cancers (pT3/4, pN+, or EMVI+) is 62%. In this setting, preoperative staging may be insufficient to allow proper identification of patients at high risk for local recurrence and/or in whom to consider alternative treatment strategies including preoperative chemotherapy or more extensive lymph node resection. Alternative preoperative staging modalities should be investigated to improve the accuracy of T, N, and EMVI status before individualized or tailored management of these patients is considered.

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