Preoperative Computerized Tomographic Assessment of Regional Lymph Node and Extramural Vascular Invasion in Colonic Cancer

Andrew T. W. McAvoy[1], Krishnan Gokul[1], Apam Chiphang[2], Dmitri Y. Artioukh[1]

Cite this article as: *McAvoy ATW, Gokul K, Chiphang A, Artioukh DY. Preoperative computerized tomographic assessment of regional lymph node and extramural vascular invasion in colonic cancer. Eurasian Med J 2018; 50: 67-70.*

ORCID IDs of the authors:
A.T.W.M. 0000-0002-0534-5468;
K.G. 0000-0002-2551-6770;
A.C. 0000-0002-8859-8291;
D.Y.A. 0000-0002-8068-4128.

[1]Department of Surgery, Southport and Ormskirk Hospital, Southport, United Kingdom
[2]Department of Radiology, Southport and Ormskirk Hospital, Southport, United Kingdom

Received: August 6, 2017
Accepted: November 22, 2017

Correspondence to: Andrew T W McAvoy
E-mail: andrew.mcavoy@hotmail.co.uk

DOI 10.5152/eurasianjmed.2018.17198

ABSTRACT

Objective: There have been recent attempts to transfer well-established principles of rectal cancer management to colonic cancer, thereby offering neoadjuvant chemotherapy to high-risk patients at least in the trial settings. Traditionally, postoperative chemotherapy is offered to patients with colonic tumors that metastasize into regional lymph nodes and have features of extramural vascular invasion (EMVI). If the same criteria are used for the selection of patients with colonic cancer for neoadjuvant chemotherapy, then their accurate preoperative detection becomes of paramount importance. The aim of the study was to establish the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the computerized tomographic (CT) assessment of lymph node involvement and EMVI in colonic cancer.

Materials and Methods: This retrospective study included 53 consecutive adult patients (35 males and 18 females; median age, 72 years) who had complete preoperative CT staging of colonic cancer followed by its surgical resection during a 12-month period from January 1, 2012, to December 31, 2012. Patients with rectal and colonic tumors presenting as an emergency who did not have complete preoperative CT imaging were excluded. Preoperative CT findings on regional lymph node status and EMVI were compared with the final histopathological staging of resected specimens calculating sensitivity, specificity, PPV, and NPV of the test.

Results: In predicting regional lymph node metastases, CT scan had a sensitivity of 85% and a specificity of 24%. PPV was calculated as 63% and NPV as 50%. In predicting EMVI, it had a sensitivity of 69% and a specificity of 49%. PPV was 37% and NPV was 78%.

Conclusion: Preoperative CT scan does not allow an accurate detection of regional lymph node metastases and EMVI and has a tendency to overstage colonic cancer.

Keywords: Colonic cancer, computerized tomography, extramural vascular invasion, neoadjuvant treatment

Introduction

Colorectal cancer is the fourth most common malignancy in the UK, with a crude incidence rate of 72 new cases for every 100,000 males and 56 for every 100,000 females, with almost three quarters of these tumors occurring in the colon [1]. Despite similar disease morphology, the treatment strategies for colonic and rectal cancer are different. In rectal cancer, neoadjuvant chemoradiation has a recognizable role aiming to downsize and/or downstage tumors that are at a risk of incomplete excision. More recently, there has been a tendency to transfer the successful and well-established principles of rectal cancer management to colonic cancer. Thus far, these took two directions mainly in the trial settings. First, more surgeons started to advocate the technique of total mesocolic excision similar to the total mesorectal excision in rectal cancer surgery [2]. Second, attempts have been made to offer neoadjuvant chemotherapy to patients with colonic cancers to improve survival, particularly in high-risk groups [3]. Traditionally, postoperative adjuvant chemotherapy has been offered to patients with colonic tumors that metastasize into regional lymph nodes (Dukes' C) and have features of extramural vascular invasion (EMVI) knowing that their 5-year survival rate does not exceed 60%–70% [1]. If the same criteria were to be used for the selection of patients with colonic cancer for neoadjuvant chemotherapy, then an accurate preoperative diagnosis of pathological regional lymphadenopathy and EMVI will become of paramount importance. Vascular spread is an important biomarker for the prediction of distant metastases. The detection of malignant cells in the intra- and peritumoral vessels may indicate the initiation of metastatic process, suggesting that systemic treatment would be beneficial in altering the prognosis.

Objectives

The aim of the study was to assess the accuracy of the computerized tomographic (CT) scan as the only widely used staging modality for colonic cancer in the preoperative detection of regional lymph node metastases and EMVI because these factors may potentially help in the selection of patients suitable for neoadjuvant chemotherapy.

Materials and Methods

All consecutive adult patients who underwent surgical resection for histologically proven invasive colonic cancer in a 12-month period between January 1, 2012, and December 31, 2012, were included. Basic demographic characteristics, including age and sex; the site of the tumor; and data on postoperative histological pTNM stage, Dukes' stage, and regional lymph node harvest were retrospectively collected. Patients with rectal and colonic tumors presenting as an emergency who did not have complete preoperative CT imaging were excluded. Preoperative thoracic and abdominal CT scan reports were also obtained, and the radiological TNM staging and EMVI status were recorded. Multi-detector CT scanner (64 slice GE scanner) was used to obtain the staging scan of the colon in the portovenous phase. An iodine-based contrast agent was injected via the intravenous route, and images were obtained 70 s post-contrast delivery. CT scans were performed with 2.5-mm slice thickness. CT characteristics of the metastatic lymph node involvement comprised its increased size (>10 mm), round as opposed to elliptical shape, irregular contour, cystic density suggestive of central necrosis, heterogenous post-contrast enhancement, and clustering of three or more lymph nodes. Regional lymph node metastases were described in accordance with the TNM classification of malignant tumors, 7th Edition, UICC [4]. The tumor was radiologically staged as N2 in the presence of more than three lymph nodes exhibiting the abovementioned characteristics. The radiological interpretation of EMVI was based on the presence of tumor "tongue" along the peritumoral veins, their stranding, nodular enlargement, or obvious blood vessel invasion (Figure 1-3). In some cases, the tumor tissue expanded the vessel, as shown in Figure 2. CT data on lymph node status and EMVI were compared with the findings on the histopathological examination of the resected specimens calculating the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) as well as the accuracy of the preoperative CT staging. This retrospective study was using previously collected hospital, radiological, operative and histological data and

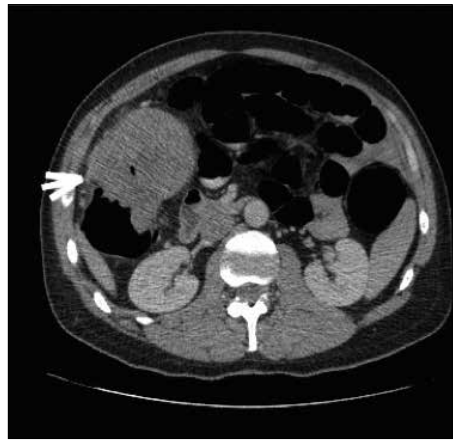

Figure 1. CT scan (axial view) showing tumor of the hepatic flexure of the colon with features of EMVI (blue arrow)

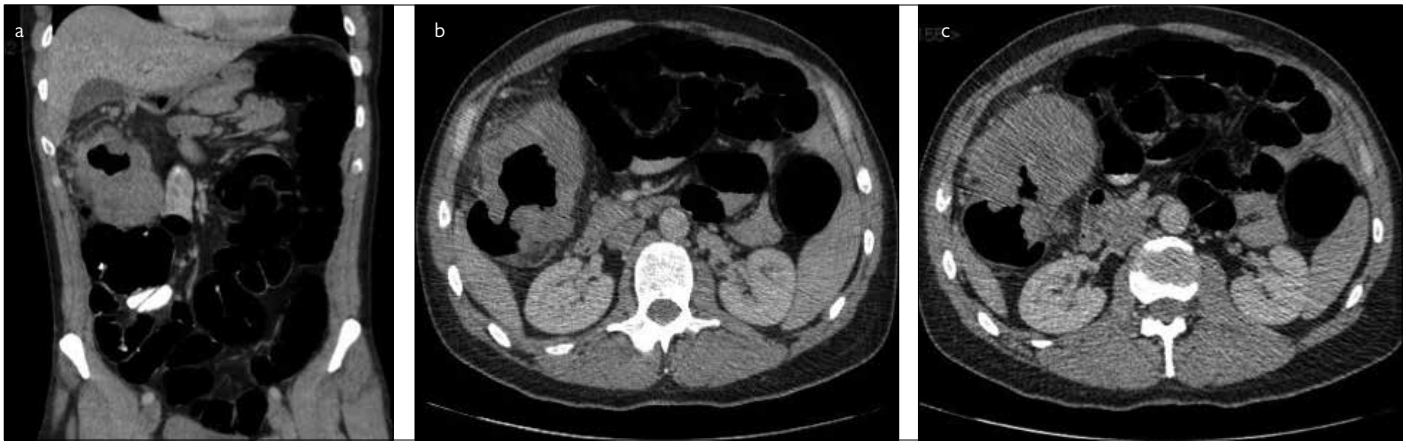

Figure 2. Coronal (a) and axial (b) CT post-contrast portovenous images of a stricturing hepatic flexure tumor with a prominent draining vessel [a key feature of extramural vascular invasion (red arrow), Axial CT portovenous phase images with nodal disease (green arrow) and hepatic flexure stricturing tumor (c)

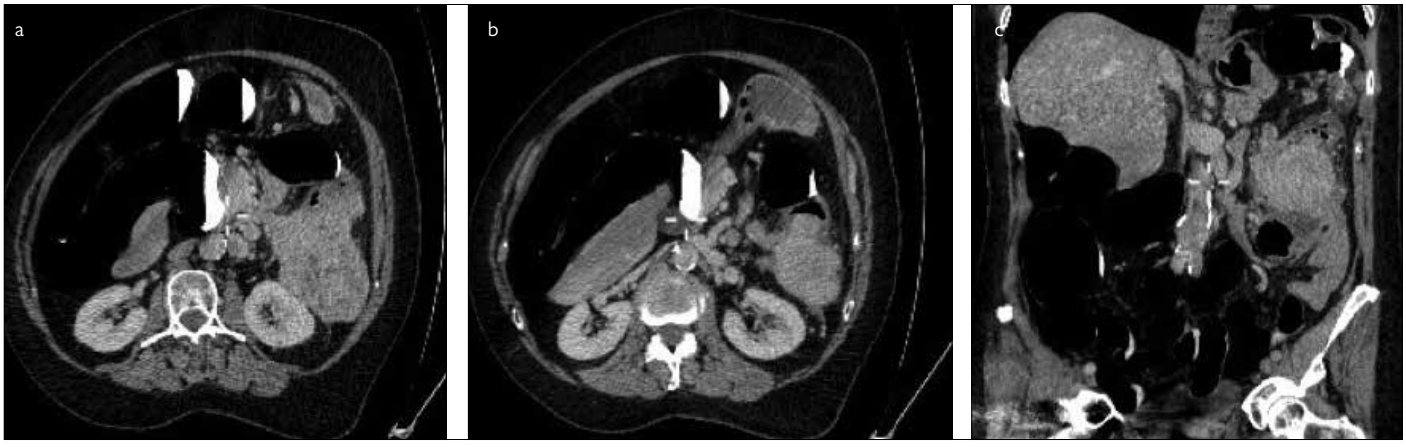

Figure 3. Axial CT portovenous phase with enlarged enhancing right retroperitoneal lymph node (green arrow) and a circumferential tumor of the descending colon (a), Axial CT in the portovenous phase (b) and coronal CT images (c) with dilated enhancing vessel and nodular outline features of extramural vascular invasion (red arrow)

did not require Ethics Committee approval. The study did not require specific consent apart from informed consent apart from informed written consent obtained from each patient at the time of surgical intervention.

Results

Fifty-three patients (35 males and 18 females) underwent resections for colonic cancer, as summarized in Table 1. Their median age was 72 (range, 46–93) years. Eleven (21%) patients had tumors located in the cecum, ten (19%) had tumors located in the ascending colon, three (6%) had tumors located in the hepatic flexure, nine (17%) had tumors located in the transverse colon, three (6%) had tumors located at the splenic flexure, three (6%) had tumors located in the descending colon, and fourteen (26%) had tumors located in the sigmoid colon. The histopathological staging was T1 in none (0%) of the patients, T2 in six (11%), T3 in 28 (53%), and T4 in 19 (36%). Lymph node status was N0 in 21 (40%), N1 in 16 (30%), and N2 in 16 (30%). The median lymph node harvest was 17 (range 5–40). Therefore, no patients had Dukes' A tumor, 21 (40%) had Dukes' B, 28 (53%) had Dukes' C, and 4 (7%) had Dukes' D cancer.

Table 1. Summary of patient and tumor characteristics

Characteristics	N=53 (%)
Age (median)	72 (46–93)
Sex	
Male	35 (66%)
Female	18 (34%)
Tumor Location	
Cecum	11(21%)
Ascending colon	10 (19%)
Hepatic flexure	3 (6%)
Transverse colon	9 (17%)
Splenic flexure	3 (6%)
Descending colon	3 (6%)
Sigmoid	14 (26%)
Tumor Stage	
T1	0
T2	6 (11%)
T3	28 (53%)
T4	19 (36%)
N0	21 (40%)
N1	16 (30%)
N2	16 (30%)
M1	4 (8%)
Dukes A	0 (0%)
Dukes B	21 (40%)
Dukes C	28 (53%)
Dukes D	4 (7%)
Median Lymph Node Yield	17 (Range: 5–40)

Table 2. Preoperative CT prediction of lymph node status and EMVI in comparison with histological examination of resected specimens

	Lymph Node Prediction	Extramural Vascular Invasion Prediction
Sensitivity	85%	69%
Specificity	24%	49%
Positive Predictive Value	63%	37%
Negative Predictive Value	50%	78%

Lymph node status prediction

CT imaging identified 43 lymph node-positive and 10 lymph node-negative patients. However, only 32 patients had histologically proven lymph node metastases. CT scan had a sensitivity of 85% and a specificity of 24% in the prediction of regional lymph node metastases. PPV was 63%, and NPV was 50% (Table 2).

Extramural vascular invasion prediction

CT imaging identified features of EMVI in 30 patients. Twenty-three patients were EMVI-negative. Postoperative histological examination revealed EMVI-positive tumors in 16 patients and EMVI-negative tumors in 37. CT prediction of EMVI had a sensitivity of 69% and a specificity of 49%. PPV was 37%, and NPV was 78% (Table 2).

Discussion

The choice of treatment of newly diagnosed malignancy depends on its accurate staging. Of the three main modalities [CT, magnetic resonance imaging (MRI), and positron emission tomography (PET)], CT and, to a lesser extent, PET scans have played the role of the exclusion of distant metastases in both colonic and rectal cancers, thereby allowing the selection of patients for potentially curative treatment. The use of MRI for the local staging of rectal tumors has greatly helped in identifying patients at a risk of incomplete tumor excision and in selecting them for neoadjuvant treatment [5]. Thus, in rectal cancer, downstaging and/or downsizing neoadjuvant chemoradiation has become a standard practice when the feasibility of complete excision is questioned because of the proximity of the tumor and/or pathologically enlarged lymph nodes to the mesorectal fascia ultimately forming the circumferential resection margin [6]. MRI has proved to be less accurate for the local staging of colonic cancer and has been of minimal clinical relevance thus far because after CT exclusion of distant metastases, the vast majority of patients with colonic cancer are offered immediate surgery. In contrast to rectal tumors, surgical resection has remained the main treatment for colonic tumors thus far, with 80% of patients receiving resection of the primary tumor as the first treatment step. Colonic resection can be followed by adjuvant chemotherapy (and occasionally radiotherapy) if adverse prognostic characteristics are identified on the histological examination of the resected specimen [7].

More recently, attempts have been made to advocate neoadjuvant chemotherapy to patients with colonic cancer [3]. Arguably, chemotherapy administered before surgery has a theoretical advantage of the early treatment of micrometastases, addresses adverse consequences of inevitable malignant cell shedding during surgical manipulation, allows better delivery of anti-neoplastic agents via undisturbed blood supply to the tumor, and is probably associated with better patient compliance [6]. Thus, neoadjuvant chemotherapy for locally advanced colonic cancer is currently being investigated by FOXTROT trial. Although the trial demonstrated downstaging in T3 and T4 tumors, neither nodal status nor the presence of EMVI was used in the inclusion criteria [3]. In addition to TNM staging, several other tumor-related factors are linked to adverse oncological outcomes, such as histological differentiation, mucin production, host lymphoid response to the tumor, tumor border configuration, absence of microsatellite instability, and loss of heterozygosity at chromosome 18q [8]. The features of EMVI and perineural invasion are also associated with adverse prognosis [9]. EMVI can be defined as the direct invasion of a blood vessel by the tumor. The presence of malignant cells in the intra- and peritumoral vessels, even if these developed because of the process of neovascularization, may indicate the initiation of systemic hematogenous spread, which indicates a poor prognosis [10] and warrants systemic chemotherapy. Angiogenesis, when proven, can also be used for targeted therapies [10].

Currently, the standard practice is to offer postoperative chemotherapy mainly to patients with histologically proven regional lymph nodes metastases and EMVI. If the same factors could be confidently established by accurate preoperative staging, then it could theoretically also aid in the selection of patients for neoadjuvant treatment.

Preoperative staging is both technology- and operator-dependent and, therefore, has variable results [11]. Currently, CT is the only practical tool for the staging of colonic cancer. Choi et al. [12] evaluated the preoperative CT assessment

of regional lymphadenopathy and reported a sensitivity of 88%, specificity of 66%, PPV of 59%, and NPV of 88%. A meta-analysis by Dighe et al. [13] included 19 studies comprising a total of 907 patients and found an overall CT sensitivity of 70% and specificity of 78% for the detection of regional lymph node involvement. The sensitivity of 85% in our series is in line with the abovementioned studies. CT detection of EMVI is even more challenging with an inter-observer variation between 54.5% and 61.0% and has reported sensitivity of 58%, specificity of 95%, and accuracy of 53% [14, 15]. Unlike in rectal cancer imaging, MRI and PET scans in colonic cancers have low sensitivity values [16-18]. Rollven et al. [16] compared high-resolution MRI with CT in the detection of the locally advanced stage, nodal, and EMVI positivity of colonic cancer and concluded that MRI may offer a slight advantage in accuracy. However, more recently, Hunter et al. [19] stated that they could not recommend that MRI should replace CT. PET/CT scan also proved to be inferior to CT scan alone in the detection of lymph node-positive disease [18].

Previous studies have suggested that the administration of neoadjuvant chemotherapy on a single criterion of the radiologically detected enlargement of the regional lymph nodes would result in overtreatment due to the lack of specificity; therefore, the search for additional indicators such as EMVI. Our results showed that the risk of neoadjuvant oncological overtreatment remained even when the selection was based on both the lymph node status and EMVI as judged on the preoperative CT scan. The future developments in this field will depend on whether the ongoing trials will prove the benefit of neoadjuvant chemotherapy to make it a standard of treatment in selected patients with colonic cancer and whether new diagnostic imaging modalities will become available to aid such a selection with more accuracy than the currently available CT scan.

In conclusion, the preoperative staging of colonic cancer by CT scan does not allow an accurate detection of regional lymph node metastases and EMVI.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - K.G., D.Y.A.; Design - K.G., D.Y.A.; Supervision - K.G., D.Y.A.; Resource - A.T.W.M., K.G., A.C., D.Y.A.; Materials - A.T.W.M., K.G., A.C., D.Y.A.; Data Collection and/or Processing - A.T.W.M., K.G.; Analysis and /or Interpretation - A.T.W.M., K.G., A.C., D.Y.A.; Literature Search - A.T.W.M., K.G.; Writing - A.T.W.M., K.G., A.C., D.Y.A.; Critical Reviews - D.Y.A.

Conflict of Interest: Authors have no conflict of interest to declare.

Financial Disclosure: The authors declare that this study has received no financial support.

References

1. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer (Accessed: 20/06/2017).
2. Hohenberger W, Weber K, Matzel K, et al. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation: technical notes and outcome. Colorectal Dis 2009; 11: 354-64. [CrossRef]
3. Foxtrot Collaborative Group. Feasibility of preoperative chemotherapy for locally advanced, operable colon cancer: the pilot phase of a randomised controlled trial. Lancet Oncol 2012; 13: 1152-60. [CrossRef]
4. Sobin LH, Gospodarowicz MK, Wittekind C, editors. TNM Classification of Malignant Tumours, 7th Edition. Wiley-Blackwell; 2011.
5. Brown G, Radcliffe AG, Newcombe RG, et al. Preoperative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. Br J Surg 2003; 90: 355-64. [CrossRef]
6. Sauer R, Becker H, Hohenberger W, et al. German Rectal Cancer Study. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 2004; 351: 1731-40. [CrossRef]
7. Quasar Collaborative Group, Gray R, Barnwell J, et al. Adjuvant chemotherapy versus observation in patients with colorectal cancer: a randomised study. Lancet 2007; 370: 2020-9. [CrossRef]
8. Wang W, Wang GQ, Sun XW, et al. Prognostic values of chromosome 18q microsatellite alterations in stage II colonic carcinoma.World J Gastroenterol 2010; 16: 6026-34.
9. Burton S, Norman AR, Brown G, et al. Predictive poor prognostic factors in colonic carcinoma. Surg Oncol 2006; 15: 71-8. [CrossRef]
10. Minsky BD, Mies C, Rich TA, et al. Potentially curative surgery of colon cancer: the influence of blood vessel invasion. J Clin Oncol 1988; 6: 119-27. [CrossRef]
11. Balthazar EJ, Megibow AJ, Hulnick D, et al. Carcinoma of the colon: detection and preoperative staging by CT. AJR Am J Roentgenol 1988; 150: 301-6. [CrossRef]
12. Choi AH, Nelson RA, Schoellhammer HF, et al. Accuracy of computed tomography in nodal staging of colon cancer patients. World J Gastrointest Surg 2015; 7: 116-22. [CrossRef]
13. Dighe S, Purkayastha S, Swift I, et al. Diagnostic precision of CT in local staging of colon cancers: a meta-analysis. Clin Radiol 2010; 65: 708-19. [CrossRef]
14. Burton S, Brown G, Bees N, et al. Accuracy of CT prediction of poor prognostic features in colonic cancer. Br J Radiol 2008; 81: 10-9. [CrossRef]
15. Norgaard A, Dam C, Jakobsen A, et al. Selection of colon cancer patients for neoadjuvant chemotherapy by preoperative CT scan. Stand J Gastroenterol 2014; 49: 202-8. [CrossRef]
16. Rollvén E, Holm T, Glimelius B, Lörinc E, Blomqvist L. Potentials of high resolution magnetic resonance imaging versus computed tomography for preoperative local staging of colon cancer. Acta Radiol 2013; 54: 722-30. [CrossRef]
17. Zerhouni EA, Rutter C, Hamilton SR, et al. CT and MR imaging in the staging of colorectal carcinoma: report of the Radiology Diagnostic Oncology Group II. Radiology 1996; 200: 443-51. [CrossRef]
18. Kwak JY, Kim JS, Kim HJ, Ha HK, Yu CS, Kim JC. Diagnostic value of FDG-PET/CT for lymph node metastasis of colorectal cancer. World J Surg 2012; 36: 1898-905. [CrossRef]
19. Hunter C, Blake H, Jeyadevan N, et al. Local staging and assessment of colon cancer with 1.5-T magnetic resonance imaging. Br J Radiol 2016; Jun 27 [Epub ahead of print]. [CrossRef]