

Preoperative staging of colorectal cancer using virtual colonoscopy: correlation with surgical results

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Abstract. – OBJECTIVE: The aim of this study was to evaluate the clinical usefulness of computed tomography colonography (CTC) in the preoperative staging in patients with abdominal pain for occlusive colorectal cancer (CRC) and to compare the results of CTC with the surgical ones.

PATIENTS AND METHODS: 127 patients with abdominal pain, iron deficiency anemia and occlusive CRC underwent a CTC examination in prone position without intravenous contrast agent and in prone position after administration of intravenous contrast medium. All the patients underwent surgery after CTC. Two radiologists with different experience analyzed the images first independently and then by consensus. They evaluated the location of the lesion, the depth of the invasion of the colon-rectal wall (T stage), lymph node involvement (N stage) and the presence or absence of distant metastasis (M stage). CTC findings were correlated with surgical outcomes.

RESULTS: The overall accuracy values for tumour localization according to consensus reading of CTC examinations in comparison to surgical results were 100% ($K = 1$, $p = 0.0001$). The overall accuracy values of agreement for T staging of reader 1, reader 2 and consensus reading of CTC examinations in comparison to surgical results were respectively 95.5% ($K = 0.876$, $p = 0.0035$), 93.3% ($K = 0.858$, $p = 0.0037$) and 97.7% ($K = 0.926$, $p = 0.0014$) for $\leq T2$; 91.3% ($K = 0.839$, $p = 0.0027$), 88.3% ($K = 0.817$, $p = 0.0031$), and 92.9% ($K = 0.894$, $p = 0.0025$) for T3; 89.6% ($K = 0.825$, $p = 0.0037$), 86.2% ($K = 0.837$, $p = 0.0032$) and 89.6% ($K = 0.821$, $p = 0.0023$) for T4. The overall accuracy values for N staging for reader 1, reader 2 and consensus reading was 90.2% ($K = 0.865$, $p = 0.0029$). The overall accuracy values for M staging of reader 1, reader 2 and consensus reading was 92% ($K = 0.875$, $p = 0.0019$).

CONCLUSIONS: CTC with is a very useful tool for accurate pre-treatment staging and localization of occlusive CRC.

Key Words:

CT colonography, Colorectal cancer, Extracolonic findings.

Introduction

Colorectal cancer (CRC) is the second cause of cancer related death in the western world, where approximately 2.7-2.8% of the population died because of CRC¹. Most CRCs develop within benign adenomatous polyps which take on average 10 years-period to transform into invasive cancer²⁻³. Five year survival is 90% if the disease is diagnosed while still localized (i.e., confined to the wall of the bowel), but only 68% for regional disease (i.e., disease with lymph node involvement), and only 10% if distant metastases are present⁴.

Conventional colonoscopy (CC) is the current standard technique for the evaluation of the entire colon. Computed tomography colonography (CTC) is regarded as a promising technique for complete evaluation of the entire volume of the colon and simultaneous assessment of extraluminal status⁵⁻⁹.

Several articles discuss the usefulness of CTC in the occlusive CRC, and focused the attention on cases of distal colon or rectal carcinoma^{10,11}. These promising results have promoted CTC as a choice for preoperative evaluation in an occlusive CRC. Conventional CT is not so accurate in determining

the depth of wall invasion or in the evaluation of tumour foci in non-enlarged lymph nodes¹². Therefore, routine preoperative assessment for local disease is generally not performed. The aim of this study was to evaluate the clinical usefulness of CTC in the preoperative staging in patients with abdominal pain for occlusive CRC and to compare the results of CTC with the surgical ones.

Patients and Methods

Patient Population

This prospective study was approved by the Ethics Review Board of our institution and all patients gave written informed consent.

From January 2009 to August 2012, 127 patients, 53 men and 27 women (mean age of 64 years and age ranging from 42 to 86 years) with abdominal pain, iron deficiency anemia and occlusive CRC underwent a CTC examination. The tumors were initially suspected by ultrasonography in three cases, with clinical suspicion including digital rectal examination in 55 patients and with a CC in 68 patients.

CTC Acquisition Protocol

Fecal "tagging" to perform a relevant CTC examination was provided by ingesting 90 mL of Gastromiro (Iopamidol) at 3.00 p.m. and another

90 mL at 5.00 p.m. followed by 1 L of water at 6.00 p. m. in the day before the exam.

CTC was performed with a 64 multi-detector row CT scanner (Somatom Sensation 64, Siemens, Erlangen, Germany). No spasmolytic or buscopan (hyoscine n-buthylbromide) were used. Room air was carefully insufflated using a manual balloon pump through a rectal enema tube of 22 G according to the patient's tolerance. Air filling and distension of the colon were evaluated initially on the CT scout before CTC. Once bowel distention was adequate, CTC was performed with two sets of images, one obtained with the patient in prone position (no contrast scan) and the second one with the patient in supine position. The supine position scanning was performed after injection of 2 ml/kg of an iodinated contrast agent (flow rate: 3 mL/sec; scanning delay: 65 sec). CT parameters were as follows: 2.5 × 1.2 mm detector collimation, 120 kV, 50 mAs (prone), 200 mAs (supine), and a pitch of 1.25. Axial CT images were reconstructed as 1-mm slices with a 1-mm reconstruction interval.

Image Interpretation

CT images were transferred to a remote PC-based workstation using commercially available software (Im3D, Turin, Italy). The post-processed images included multiplanar reformatting (MPR), volume rendering (VR) and virtual colonoscopy images (Figures 1 and 2).

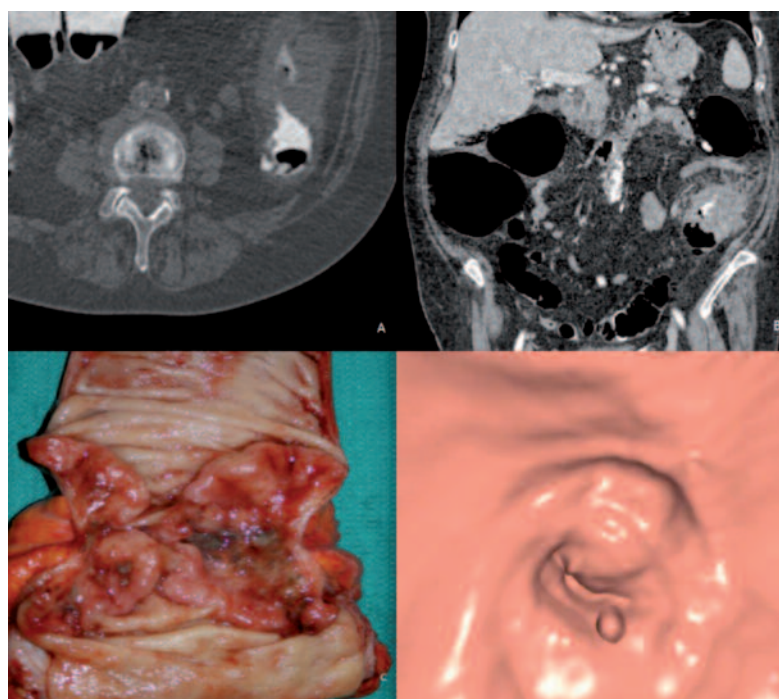
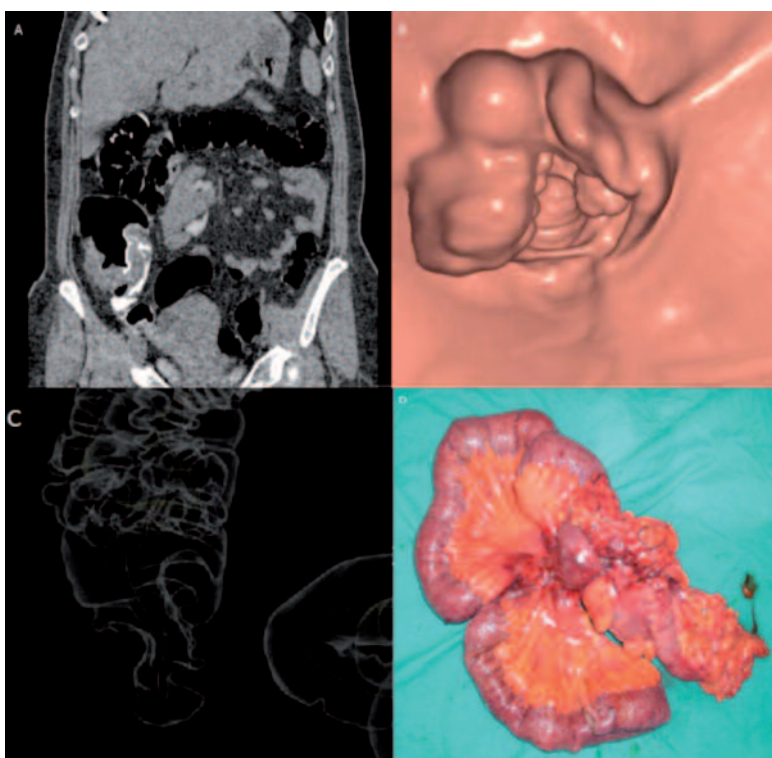


Figure 1. A 65 years-old-man with occlusive colon cancer in the descending colon. (A e B) Axial and Coronal images of colon cancer with invasion of the fatty tissue of abdomen (T3); (C) Surgical macroscopic image of the tumor. (D) endoluminal CTC image clearly showing the lesion.

Figure 2. A 49 year-old-woman with occlusive colon cancer in the cecum. **A**, Coronal image of colon cancer with invasion of the fatty tissue of abdomen (T3); **B**, endoluminal CTC image clearly showing the lesion; **C**, The virtual double-contrast enema displays an annular circumferential mass in the cecum. **D**, Surgical macroscopic image of the tumor.



Two radiologists with different experience in gastrointestinal imaging (A.S. with 7 years of experience, F.B. with 2 years of experience) analyzed independently the native images and post-processed ones during four consecutive reading sessions. In the first reading session they evaluated the location of the lesion and the depth of the invasion of the colon-rectal wall (T stage) classifying afterwards the tumour into \leq T2, T3 or T4. The lesion was considered to be T2 if it did not extend beyond the muscularis propria; T3 if it extended beyond the muscularis propria and T4 if it penetrated the visceral peritoneum or directly invaded or was adherent to other organs or structures.

During the second session the radiologists assessed the N staging (pathological involvement of lymph nodes or tumour-free lymph nodes). The tumour was deemed to be N+ if a lymph node greater than one centimeter in size or a cluster of three or more lymph nodes, regardless of their size, were encountered.

In the third evaluating session they rated the presence or the absence of distant metastasis (M staging).

In the fourth session they reassessed the images in consensus for TNM staging.

In the last reading session, performed after 1 week, the specialists reassessed the images in order to calculate the intraobserver variability for TNM staging.

Additional extraluminal findings were also analyzed. Postoperative CC was not performed to control the CTC findings and all the patients went to surgery after CTC.

Surgical resection was performed after multidisciplinary team planning with surgeons, internists, and radiologists. We retrospectively analysed the surgical outcomes and correlated CTC findings with the histopathologic findings, including the accuracy of CTC for localization of the main tumour and for TNM staging.

Statistical Analysis

Data were evaluated using a statistical analysis software (SPSS®, Statistical Package for Social Science, IBM Corporation, Armonk, NY, USA). The interobserver variability between the two radiologists and the agreement with surgical results were evaluated using Cohen's kappa statistic. A kappa value of 0.4 or less was regarded as slight agreement, 0.41 to 0.60 as moderate, 0.61 to 0.80 as substantial and 0.81 or more as almost perfect. The significance was set at $p \leq 0.05$.

The intraclass correlation coefficient (ICC) was used to evaluate intraobserver variability.

Results

The localization of the CRC according to reader 1, reader 2, consensus reading and surgery is summarized in Table I.

The agreement between the two specialists in evaluating the localization of the tumour in cecum, ascending colon and transverse colon was $K = 1$ ($p = 0.0000$), in descending colon $K = 0.912$ ($p = 0.0028$), in sigmoid colon $K = 0.938$ ($p = 0.0015$), and in the rectum $K = 0.853$ ($p = 0.0029$).

The overall accuracy values for tumour localization according to consensus reading of CTC examinations in comparison to surgical results were 100% ($K = 1$, $p = 0.0000$). CT colonography provided a quite precise information on tumour location.

A total of seven synchronous adenocarcinomas were confirmed at surgery: four in the colon proximal to the occlusion and five distal to the occlusion. All of them were correctly diagnosed preoperatively by CTC.

The TNM staging according to reader 1, reader 2, consensus reading and surgery is showed in Table II.

The overall accuracy values of agreement for T staging of reader 1, reader 2 and consensus reading of CTC examinations in comparison to surgical results were respectively 95.5% ($K = 0.876$, $p = 0.0035$), 93.3% ($K = 0.858$, $p = 0.0037$) and 97.7% ($K = 0.926$, $p = 0.0014$) for $\leq T2$; 91.3% ($K = 0.839$, $p = 0.0027$), 88.3% ($K = 0.817$, $p = 0.0031$), and 92.9% ($K = 0.894$, $p = 0.0025$) for T3 (Figures 1, 2); 89.6% ($K = 0.825$, $p = 0.0037$), 86.2% ($K = 0.837$, $p = 0.0032$) and 89.6% ($K = 0.821$, $p = 0.0023$) for T4. Three of 29 T4 lesions were understaged at CTC due to inadequate distension ($n = 1$) and misinterpretation of adjacent organ involvement as partial volume averaging ($n = 2$). The overall accuracy values for N staging for reader 1, reader 2 and consensus reading was 90.2% ($K = 0.865$, $p = 0.0029$). 16 patients (12.5%) were overstaged and 5 patients (3.9%) were understaged at CTC.

The overall accuracy values for M staging of reader 1, reader 2 and consensus reading was 92% ($K = 0.875$, $p = 0.0019$). In three patients a liver metastasis was detected only during surgery thanks to intraoperative ultrasound; these lesions

were not depicted on CTC images neither during a retrospective consensus reading because of their too small size.

The intraobserver variability was ICC = .994 in reader A and ICC = .989 in reader B.

Discussion

At present, CT is regarded as a routine procedure for preoperative evaluation in patients suspected of having advanced CRC⁶⁻⁸. Mauchley et al¹³ suggest that routine preoperative CT provides informations that definitely change treatment in 16% of patients with a good cost-effectiveness. The accuracy of T staging by CT is also not satisfactory, ranging from 53 to 77%⁸⁻¹². Recent multi-detector row CT (MDCT) scanners allow thinner collimation, resulting in marked improvement of scanning resolution. Therefore, MDCT with virtual endoscopy and multiplanar reformation could improve the accuracy of preoperative TNM staging with whole body evaluation¹⁴⁻¹⁶. In our study, the overall accuracy of T staging in consensus reading was 97.7% for $\leq T2$, 92.9% for T3 and 89.6% for T4, the overall accuracy of N staging and M staging was 90.2% and 92% respectively.

Total large bowel evaluation is important in planning the treatment of patients with CRC because synchronous adenomas and adenocarcinomas are found respectively in 14-48% and 2-9% of cases^{17,18}. We found a total of seven synchronous adenocarcinomas diagnosed preoperatively by CTC and all of them were confirmed at surgery. Although conventional colonoscopy is regarded as the gold standard for the evaluation of the colon for colorectal tumors, it may be incomplete due to tumor obstruction, that is a frequent event in distal cancers, dolichocolon or inflammatory stricture due especially to diverticulitis^{3,19}.

We observed many cases in which at CC lesions seemed to be in the proximal colon while at CTC they were distal colonic lesions. Several articles report that CC has a considerable error rate for localization of CRC and is inaccurate in 11-21% of case^{20,21}. Anatomic variation and the absence of fixed internal landmarks make it difficult to localize the tumour accurately. Furthermore, in occlusive colon cancer, tumour localization may be more difficult, even for experienced endoscopists, because inferring the tumour location from the ileo-cecal valve is impossible. Con-

Table I. Localization of the CRC according to reader 1, reader 2, consensus reading and surgery.

Location	Reader 1	Reader 2	Consensus reading	Surgery
Cecum	33	33	33	33
Ascending colon	16	16	16	16
Transverse colon	18	18	18	18
Descending colon	24	22	23	23
Sigmoid colon	28	27	27	27
Rectum	8	11	10	10

ventional colonoscopy was inaccurate for tumour localization in 21% of occlusive CRC cases, and there were clinically significant localization errors in 11% of occlusive CRC cases that required modification of surgical approach.

Accurate tumour localization for rectal carcinomas also has substantial clinical importance for preventing the inappropriate use of adjuvant therapy and determining the proper surgery, such as segmental sigmoid resection, low anterior resection, or abdominoperineal resection²². Preservation of the anal sphincter is dependent on the distance between the lower edge of the tumour and the external sphincter and levator ani muscle. CTC may provide an objective measurement of the distance of the tumour from the anal verge, which is mandatory for rectal surgery.

Concerning TNM staging, the biggest problem in our study was found in N staging, because many patients with lymph nodes larger than 1 cm in size were classified as pathological, but did not show pathological changes at the postoperative histological examination. On the contrary, some lymph nodes smaller than 1 cm in size were rated negative, but showed tumour metastases at the postoperative histological examination. In our study, 83.6% of patients with lymph node involvement were correctly staged, 12.5% were overstaged and 3.9% were understaged by CTC. In all overstaged cases, overstaging was caused

by the presence of reactive nodes larger than 1 cm. Although the superiority of MRI in the detection of lymph node involvement has been documented in early reports, Ergen et al. report poor agreement between MRI and surgical-pathologic staging for lymph node involvement^{22,23}; however, the role of MDCT and MRI in the assessment of regional lymph node involvement has not been evaluated in large clinical series. Until now there is no solid evidence to support the routine clinical application of 18F-FDG PET/CT in the pretherapeutic evaluation of lymph node status in patients with CRC²⁴. However, 18F-FDG PET/CT could be used to strengthen the possibility of suspected metastatic lymph nodes detected by other imaging modalities²⁵.

As regards extracolonic findings, published studies have tended to report the frequency of extracolonic findings in terms of “moderate importance” and “high importance” (with “low importance” generally assumed to represent a clinically insignificant finding)²⁶⁻³⁰. In our caseload excluding all those injuries seen in stage N+ and M+, in two cases the presence of high important extracolonic findings has modified the planning of the surgical intervention: in one patient a right pelvic kidney with abnormal course of the ureter passing close to the surgical area was discovered; in the second, intussusception on a chronic inflammatory bowel disease was found.

Table II. TNM staging according to reader 1, reader 2, consensus reading and surgery.

TNM staging	Reader 1	Reader 2	Consensus reading	Surgery
≤ T2	43	42	44	45
T3	58	60	57	53
T4	26	25	26	29
N+	102	102	102	113
N-	25	25	25	14
M+	23	23	23	26
N-	104	104	104	101

Conclusions

CTC can provide an accurate CRC localization, tumour extent, tumour/nodal staging, and extra-colic abnormalities, which are critical for the proper management of patients. As a result, CTC may become a modality of choice for pre-operative evaluation of all colorectal cancers. CTC with “fecal tagging” approach is a very useful tool for accurate pre-treatment staging and localization of occlusive CRC.

Conflict of interest

The authors declare that there is no conflict of interest.

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