



## Over-diagnosis for preoperative T staging of colorectal cancer - A case series

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### ABSTRACT

**Introduction:** Recent progressive imaging technology such as multiplanar reconstruction on computed tomography (CT) and colonoscopy has made preoperative T staging of colorectal cancer (CRC) more accurate. Nevertheless, it is still difficult to make a correct diagnosis in some cases. The aim of this case study was to investigate the accuracy of T staging diagnosis in patients with CRC who underwent curative operations and to identify the causes of preoperative over-diagnosis.

**Method:** Medical charts of 1013 colorectal cancer patients who underwent a curative operation in the University of Tokyo Hospital between January 2011 and December 2016 were analyzed retrospectively. We defined a two-level or more difference between clinical and pathological T stages as over-diagnosis or under-diagnosis.

**Results:** Nine patients were over-diagnosed in T stage preoperatively. The rate of over-diagnosis was 0.9%. At least three main factors for over-diagnosis were identified: close-to-circumferential or obstructive lesion; a rough appearance in the adipose tissues around the tumor on CT; and a tumor with a depressed structure.

**Conclusions:** Clinical T stage is overestimated with a marked difference from pathological T stage in approximately 1% of CRC patients. Further progress in diagnostic modalities is required for more accurate staging.

### 1. Introduction

The accuracy of preoperative T staging is reported as 57–93% since the technology of imaging devices has developed [1–6]. In our hospital, we routinely perform colonoscopy, multidetector CT with three-dimensional angiography, and CT-colonography (CTC) or contrast enema for all patients with CRC [7,8]. With these image results, we diagnose the preoperative stage, which is used to determine the operative procedure. Nevertheless, the clinical and pathological diagnoses for the depth of tumor invasion (T stage) occasionally differ. In this study, we reviewed over 1000 CRC patients in our department. We report CRC patients who were over-diagnosed preoperatively and discuss what caused the over-diagnosis in T stage.

### 2. Materials and methods

We retrieved the medical records of 1013 consecutive patients with CRC who underwent curative operations in the University of Tokyo Hospital between January 2011 and December 2016. Patients treated with endoscopic submucosal dissection (ESD), endoscopic mucosal resection, neoadjuvant chemotherapy or radiation therapy, as well as recurrent cancer and rectal cancer below the peritoneal reflection were excluded from this analysis. The patients' clinical stages were diagnosed

at a multidisciplinary meeting by gastrointestinal surgeons and radiologists. Here we classified clinical and pathological T into five stages, namely Tis, T1, T2, T3 and T4, essentially based on the AJCC/TNM classification [9]. We defined a two-level or more difference between clinical and pathological T stages as over-diagnosis or under-diagnosis.

The study was conducted in accordance to Declaration of Helsinki for human research, registered under Research Registry (Researchregistry3406) and reported in line with the PROCESS criteria [10]. Written informed consent was obtained from the patients for publication of this article and any accompanying images.

### 3. Results

#### 3.1. General findings

The rate of over-diagnosis was 0.9% (9/1013) and the rate of under-diagnosis 1.2% (12/1013). Table 1 shows the correlation between clinical and pathological T stages in our study. Table 2 summarizes the details of the nine patients whose T stage was over-diagnosed preoperatively. They were staged by CT, colonoscopy, CTC, and/or contrast enema. When determining preoperative T stage, we generally pay attention to a rough appearance in the adipose tissues around the tumor on CT, intestinal wall deformities with CTC or contrast enema, and the

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**Table 1**  
Correlation between clinical and pathological T stages.

Clinical T stage	Pathological T stage					Total
	Tis	T1	T2	T3	T4	
Tis	5	2	0	0	0	7
T1	9	123	25	1	1	159
T2	2	40	73	79	11	205
T3	0	6	46	285	166	503
T4	1	0	0	55	83	139
Total	17	171	144	420	261	1013

**Table 2**  
Summary of the nine patients who exhibited a difference between clinical and pathological T stages.

Patients no., sex/age (y.o.)	Location	cT	pT	Methods of diagnosis	Major findings	Pattern
1. F/71	Descending colon	T3	T1	Colonoscopy, CT, CTC	100% circumference	A
2. F/69	Sigmoid colon	T4	Tis	Colonoscopy, CT, Contrast enema	100% circumference Raised CT density Many diverticula	A, B
3. F/83	Ascending colon	T3	T1	Colonoscopy, CT, CTC	50% circumference 37 mm in size	A
4. F/86	Sigmoid colon	T3	T1	Colonoscopy, CT, CTC	50% circumference Raised CT density 53 mm in size	A, B
5. F/80	Sigmoid colon	T3	T1	Colonoscopy, CT, CTC	Raised CT density	B
6. F/76	Ascending colon	T3	T1	Colonoscopy, CT, CTC	50% circumference 75 mm in size	A
7. F/75	Cecum	T3	T1	Colonoscopy, CT, CTC	Raised CT density	B
8. M/58	Rectosigmoid colon	T2	Tis	Colonoscopy, CT, Contrast enema	Tumor with depression	C
9. M/69	Sigmoid colon	T2	Tis	Colonoscopy, CT, CTC	Tumor with depression 35 mm in size	C

yo., years old; cT, clinical T; CTC, CT colonography; F, female; M, male; pT, pathological T.

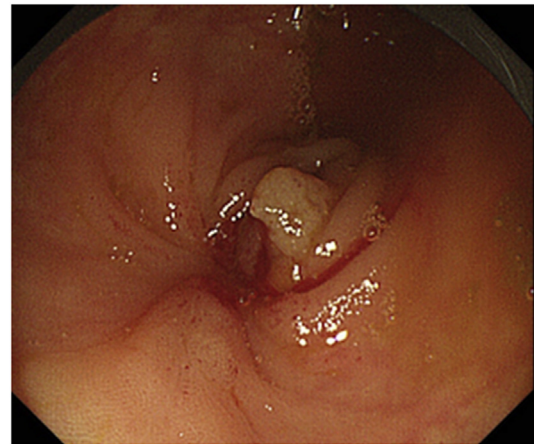
circumferential extent and structure of the tumor with colonoscopy. At least three reasons for the over-diagnosis were identified. The first was a close-to-circumferential or obstructive lesion revealed by colonoscopy and/or CTC or contrast enema (Pattern A). Five patients showed Pattern A; all of them were diagnosed with preoperative T3 and turned out to have pathological T1 stage.

The second was a rough appearance in the adipose tissues around the tumor on CT (Pattern B). Four patients showed Pattern B; all of them were diagnosed with preoperative T3 and turned out to have pathological Tis or T1. Two patients had both Pattern A and B.

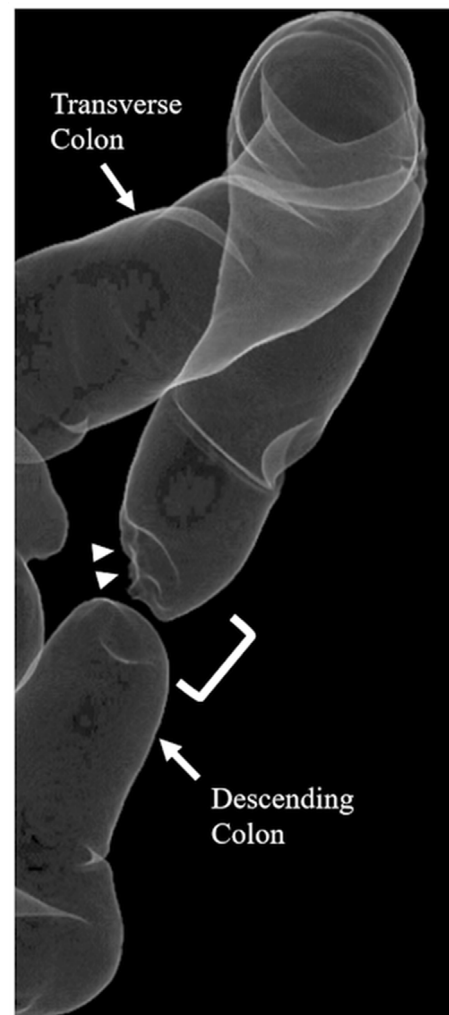
The third reason was a protruding tumor with depressed structure (Pattern C). Two patients showed Pattern C with clinical T2 cancer, who were then pathologically diagnosed with Tis.

**3.2. Case presentation**

We first present a representative case of Pattern A (Case 1). A 71-year-old woman underwent ESD for early colon cancer in the transverse colon. A follow-up colonoscopy after a 3-year interval revealed severe

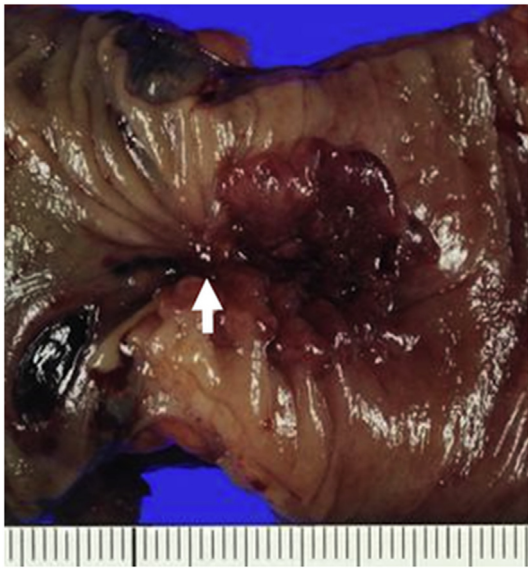


**Fig. 1.** Colonoscopy shows a bowel obstruction at the descending colon in Case 1.



**Fig. 2.** CTC shows severe narrowing in the descending colon (bracket) and a wall deformity at the oral side (arrowheads) (Case 1).

narrowing at the descending colon but the appearance of the mucosa looked normal in the region (Fig. 1). CTC revealed a bowel obstruction at the descending colon near the splenic flexure and a wall deformity at the oral side of the bowel obstruction (Fig. 2). There was no rough appearance in the adipose tissues around the tumor on CT. The patient



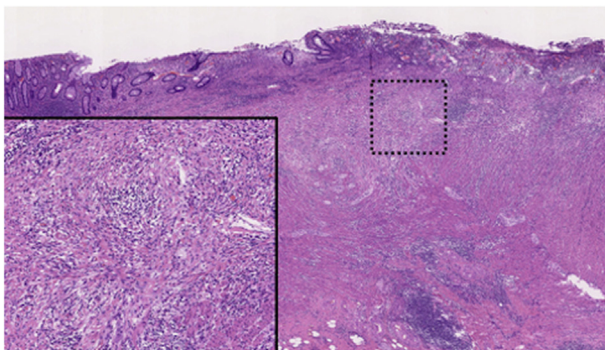
**Fig. 3.** The obstructive site is close to the anal edge of the tumor (arrow) (Case 1).

was diagnosed with a clinical T3 colon cancer.

Left hemicolectomy was performed via a laparoscopic approach. A 20 × 20 mm tumor with superficial elevated and depressed morphology was histopathologically composed of well-differentiated tubular adenocarcinoma that invaded into the submucosal layer (pathological T1 stage) without lymphatic or venous invasion. No metastasis was found in the dissected regional lymph nodes. Close to the anal end of the tumor, a stricture was prominent (Fig. 3), where only fibrosis was observed without malignant cell infiltration (Fig. 4).

Next, we present a representative case of Pattern B (Case 2). A 69-year-old woman underwent colonoscopy because of positive occult blood. Her serum level of C-reactive protein was high at 8.66 mg/dl and her white blood cell count was 6900/μl on admission, although she did not complain of fever or abdominal pain. A colonoscopy revealed a protruding tumor approximately 3 cm in size at the sigmoid colon (Fig. 5). Contrast medium and air barely passed through the lesion on contrast enema (Fig. 6). CT revealed a rough appearance in the adipose tissues and the wall thickness around the tumor (Fig. 7). We diagnosed the tumor as T4 stage preoperatively.

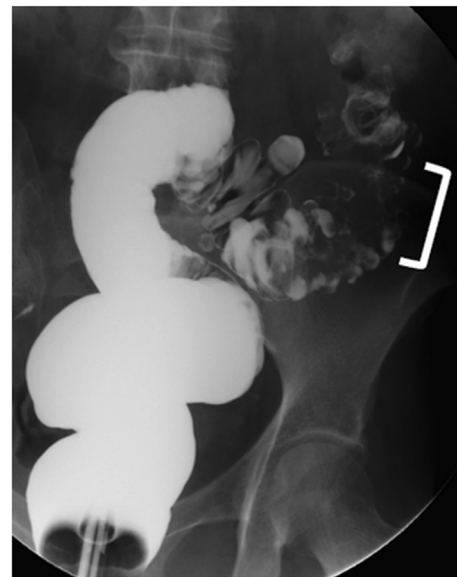
Sigmoid colectomy was performed via a laparoscopic approach. A 21 × 18 mm tumor with a stalk was histopathologically composed of tubular adenocarcinoma limited within the mucosa without lymphatic and venous invasion (pathological Tis stage). No metastasis was found



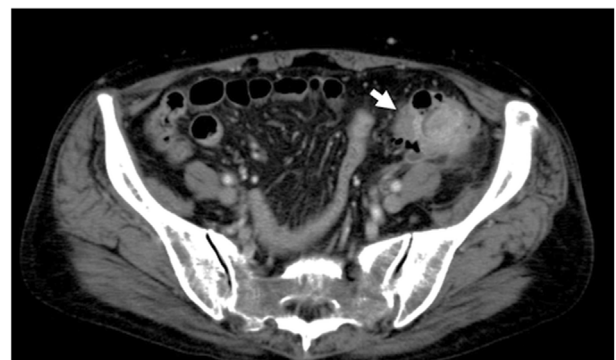
**Fig. 4.** The histopathological findings show only fibrosis without malignant cell invasion at the obstruction in Case 1 (H&E staining, original magnification: ×20). Inset shows a magnified view of the square area marked by the dashed line (original magnification: ×100).



**Fig. 5.** Colonoscopy shows a lumen-occupying protruding tumor approximately 3 cm in size in the sigmoid colon in Case 2.



**Fig. 6.** Contrast medium and air can barely pass through the tumor (bracket) on contrast enema (Case 2).



**Fig. 7.** CT scans show the rough appearance in the adipose tissues around the tumor (arrow) (Case 2).

in the dissected regional lymph nodes.

#### 4. Discussion

We investigated the accuracy of preoperative diagnosis of T staging



in 1013 consecutive CRC patients who underwent curative operations. The accuracy of preoperative T staging is improved as the technology of imaging devices are developed. So et al. showed that the rate of one-level over-diagnosis between clinical and pathological T stage was 16.8% (48/285) and the rate of two-level or more over-diagnosis was 5.3% (15/285) with CT [11]. In this study, the rate of one-level over-diagnosis was 14.8% (150/1013) and the rate of two-levels or more over-diagnosis was 0.9% (9/1013) with CT, colonoscopy, CTC, and/or contrast enema. Colonoscopy, CTC, and contrast enema improve the accuracy of preoperative T stage.

As shown in Table 2, we found at least three patterns associated with over-diagnosis. Regarding a close-to-circumferential or obstructive lesion (Pattern A), Yang et al. reported that 97.3% of obstructive CRCs (209/215) were at pathological T2 or higher stage [12]. Furthermore, Horie et al. reported that 91.2% of rectal cancers with a circumferential extent of 50% or more evaluated by CTC and colonoscopy were diagnosed as pathological T3/T4 [13]. These findings suggest that there are still a small proportion of CRCs invading only to the submucosal layer. Pattern A was a major factor for over-diagnosis (5 out of 9 cases) in this study.

For the rough appearance in the adipose tissues around the tumor on CT (Pattern B), Utano et al. reported that the positive predictive value of T3/T4 was 96.3% [14]. In contrast, Hulsmans et al. reported that not only T4 invasion but also inflammatory reactions and extramural fibrosis can cause a rough appearance [15]. Pattern B was the second leading cause in this study.

The depth diagnosis of a protruding tumor with a depressed structure has been investigated mainly based on endoscopic features. Tumors with a depressed structure generally have a tendency for deep invasion despite their small size [16]. Kobayashi et al. reported that the frequency of pTis was 1.3% in CRCs with preoperative T2 diagnosed by colonoscopy [17]. In this study, two tumors with depressed structure were diagnosed as preoperative T2 that turned out to be pathological Tis.

Our study has several limitations. First, this was a retrospective study. Second, this was a single-center study with a small sample size. Other patterns would be found by a larger sample size.

In conclusion, we identified at least three reasons for over-diagnosis namely a close-to-circumferential or obstructive lesion, a rough appearance in the adipose tissues around the tumor on CT, and a protruding tumor with a depression. Recent advances in preoperative imaging modalities have increased the diagnostic reliability of preoperative T stage to an acceptable level. Nevertheless, there are still some patients who show a marked discrepancy between clinical and pathological T stages. Therefore, diagnostic accuracy in preoperative staging still needs to be improved.

### Ethical approval

All procedures performed in studies involving human participants were in accordance with the Ethics Committees of the University of Tokyo (No.3252-(5)). Written informed consent was obtained from all patients for the publication of this case report and accompanying images.

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### Author contribution

YH wrote the manuscript. YH, HN, KK, KH, TT, TN, KO, KS, MK, and SE acquired the clinical and pathological data. HN and KM contributed to editing the manuscript. All authors read and approved the final manuscript.

### Conflicts of interest

All the authors declare that they have no competing interests.

### Research registration number

Our research was registered at <http://www.researchregistry.com>. The name of the registry is researchregistry3406.

### Guarantor

Yugo Hirata.

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