# Characteristics of colorectal cancer diagnosed with screening abdominal ultrasonography

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Received January 4, 2016; Accepted April 8, 2016

DOI: 10.3892/mco.2016.903

**Abstract.** Patient records were retrospectively analyzed to elucidate the characteristics of patients with colorectal cancer (CRC) diagnosed with screening abdominal ultrasound (US). Patients diagnosed with CRC using abdominal US [localized irregular wall thickening (W) or a hypoechoic mass with a hyperechoic mass (M)] were enrolled. The patients were subjected to colonoscopy and treated surgically between March, 2010 and January, 2015. A total of 5 men (aged 74.0±0.8 years) and 10 women (aged 73.0±12.0 years) were analyzed. Stratification was analyzed with abdominal US. The threshold value of wall thickness to diagnose CRC was investigated with receiver operating characteristic (ROC) curve analysis. The average wall thickness was 2.8±0.4 mm in the surrounding normal tissue and 12.7±5.2 mm in CRC (one-way analysis of variance, P<0.0001). The wall was significantly thicker in CRC compared with the normal colonic wall. The calculated threshold value was 4.3 mm for the diagnosis of CRC. Stratification was preserved in W, while it was lost in M (Chi-squared test, P=0.0196). The hemoglobin concentration was lower, while the C-reactive protein, carcinoembryonic antigen and carbohydrate antigen 19-9 levels were elevated above normal values. The threshold value was 4.3 mm for the diagnosis of CRC with abdominal US.

## Introduction

Colorectal cancer (CRC) is frequently encountered in clinical practice (1). The majority of CRCs develop slowly from colon polyps, due to the adenoma-carcinoma sequence (2). To improve the prognosis of patients with CRC, prompt and accurate diagnosis is crucial. CRC is screened with fecal occult blood testing and diagnosed with colonoscopy (3). However, fecal occult blood testing is not entirely reliable, although no other modalities surpass this test regarding practicality and affordability (4). Colonoscopy is the gold standard of diagnostic methods for CRC. However, colonoscopy is not available to all patients, as not many clinicians are adequately skilled to perform this procedure (5).

Abdominal ultrasound (US) is useful for the safe and easy diagnosis of CRC patients (6-9). CRC is occasionally diagnosed with abdominal US during investigation of patients with abdominal symptoms or anemia (9). A thickened colonic wall is a clue to the diagnosis of CRC (10). The threshold value for the diagnosis of CRC, however, has not yet been determined. Stratification and contour illustrated with abdominal US are associated with the depth of invasion, either to the subserosa (SS) or the subserosa (SE) (11). If stratification and contour are associated with the morphology of CRC, such as wall thickness (W) or mass (M), morphology may designate the depth of invasion (11).

We retrospectively investigated patient records to determine the characteristics of CRC diagnosed with screening abdominal US. Blood test variables were also analyzed to assess patient backgrounds.

## Patients and methods

*Ethics statement*. This study was approved by the National Hospital Organization Shimoshizu Hospital Ethics Committee. This was not considered to be a clinical trial, as the procedures were performed as a part of routine clinical practice. Written informed consent was obtained from the patients to perform colonoscpy. Informed consent was obtained to perform abdominal US, but written forms were waived. Written informed consent for inclusion in the study was waived, as patient records were anonymized and retrospectively analyzed.

*Patients*. The medical records of patients who were treated at the National Hospital Organization Shimoshizu Hospital from March, 2010 to January, 2015 were retrospectively analyzed. Enrolled patients were required to meet the following inclusion

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*Key words:* receiver operating characteristic curve, stratification, contour, carcinoembryonic antigen, carbohydrate antigen 19-9

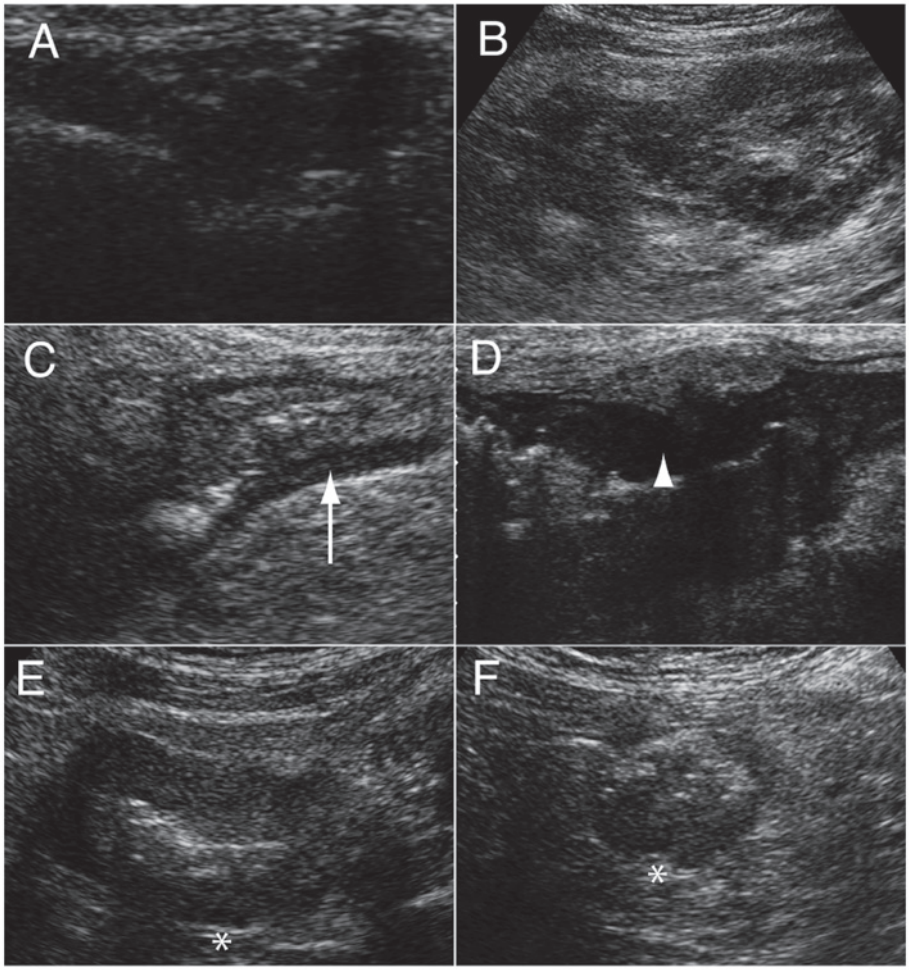


Figure 1. Morphological characteristics of colorectal cancer (CRC). CRCs were divided into two groups according to the morphological findings. The shape of CRC was classified as (A) wall thickening or (B) mass. Stratification was classified as (C) preserved (arrow) or (D) lost (arrowhead). The contour of the surface of the serosa in CRC (asterisks) was classified as (E) smooth or (F) irregular.

criteria: Subjected to abdominal US prior to colonoscopy, computed tomography (CT), or magnetic resonance imaging; underwent surgery at the National Hospital Organization Shimoshisu Hospital; and diagnosis pathologically confirmed. The patients underwent abdominal US for anemia, abdominal pain and bowel obstruction. Certain patients were subjected to abdominal US for screening. Following diagnosis of CRC with abdominal US, colonoscopy was performed in all the patients. The exclusion criteria were as follows: Subjected to abdominal US after the diagnosis of CRC with colonoscopy; subjected to abdominal US with the suspicion of CRC with CT or magnetic resonance imaging; and not subjected to surgery. The enrolled patients were restricted to those whose surgical specimens were available to investigate the depth of invasion. The enrolled patients included 5 men (aged 74.0±0.8 years) and 10 women (aged 73.0±12.0 years).

*Abdominal US*. Abdominal US was performed by Senior Fellows of the Japan Society of Ultrasonics in Medicine (M.T. and F.S) using the SSA-700A diagnostic US system (Toshiba Medical Systems Corporation, Ohtawara, Japan) with a 3.75-MHz curved-array probe (PVT-375BT; Toshiba Medical Systems) or an 8.0-MHz linear-array probe (PLT-805AT; Toshiba Medical Systems) in the US unit. The small and large intestines were scanned following routine abdominal US when intestinal diseases, such as ileus, were suspected, or when the patients had anemia.

*Criteria for the diagnosis of CRC*. The diagnostic criterion for CRC was localized irregular wall thickening (Fig. 1A) or a hypoechoic mass with a hyperechoic mass (pseudokidney sign; Fig. 1B) (10). The former is a common finding in patients with CRC (12), while the latter represents tumor tissue and air in the residual lumen (13).

*Wall thickness, shape, stratification and contour of CRC*. Wall thickness was measured with abdominal US between the mucosa and serosa borders. Wall thickness was analyzed to differentiate between CRC and the surrounding normal colonic wall. The US findings were evaluated in terms of shape, stratification and contour. Shape was divided into wall thickening (W; Fig. 1A) and mass (M; Fig. 1B). Stratification was observed due to the different layers of the colonic wall (12) and patients were divided into two groups, namely preserved (Fig. 1C) or lost stratification (Fig. 1D). Irregular contour is considered to be an US characteristic of CRC (10). A proportion of the patients had a smooth contour (Fig. 1E), while the majority exhibited irregular contour (Fig. 1F).

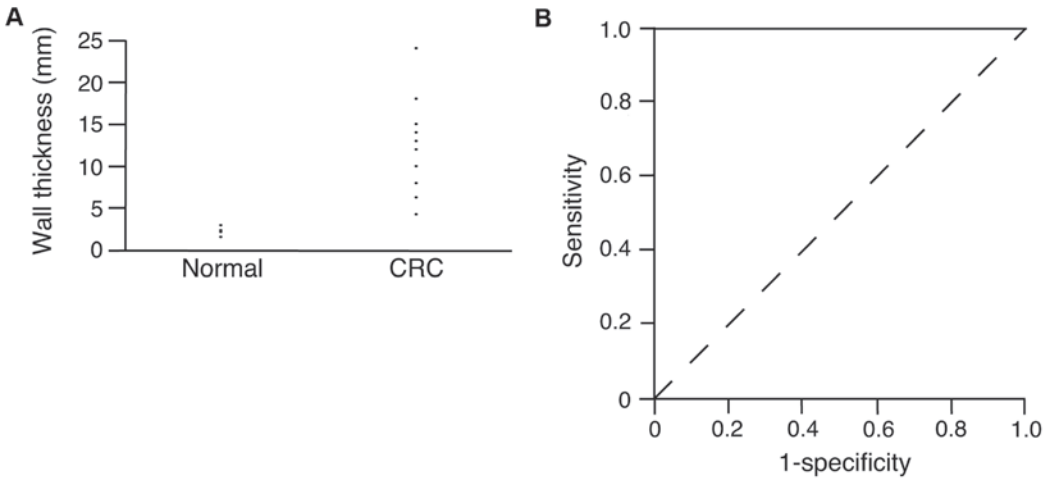


Figure 2. Scattered plot and receiver operating characteristic (ROC) curve analysis of wall thickness in colorectal cancer (CRC). (A) Wall thickness in CRC and the surrounding normal colonic wall. (B) The ROC curve corresponds to the vertical axis and upper limit line. The broken line shows the reference line.

*Pathological analysis*. The depth of invasion was determined by two pathologists (K.F. and T.K). The analyzed specimens were obtained via surgical resection. Patients referred to other hospitals for pathological analysis and those treated conservatively were excluded from the analysis.

*Blood test variables*. The blood test variables analyzed were white blood cell count, hemoglobin (Hb), C-reactive protein (CRP), carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9).

*Statistical analysis*. The mean wall thickness was compared between CRC and the surrounding normal colonic wall with one-way analysis of variance. The Chi-square test was applied to analyze the correlation between the shape of CRC (W or M) and stratification or contour. The Chi-squared test was also applied to analyze the correlation between depth of invasion and the shape of CRC (W or M), stratification, or contour. The threshold value of wall thickness to diagnose CRC was investigated with receiver operating characteristic (ROC) curve analysis. A P-value of <0.05 indicated statistically significant differences. JMP 10.0.2 software (SAS Institute, Cary, NC) was used for all statistical analyses.

## Results

*Comparison of wall thickness between CRC and normal colon*. The wall thickness in CRC and in the surrounding normal colonic wall was measured and plotted in Fig. 2A. The average wall thickness was 2.8±0.4 mm in the surrounding normal tissue and 12.7±5.2 mm in CRC. The wall was significantly thicker in CRC compared with the normal colonic wall (P<0.0001). The thickness of normal colonic wall was <3.0 mm, while it was >4.3 mm in CRC. As shown in Fig. 2A, there may be a threshold value for the diagnosis of CRC using wall thickness. ROC curve analysis was performed to investigate the threshold value for the diagnosis of CRC using abdominal US. The calculated threshold value was 4.3 mm. The sensitivity and specificity at this value were both 100%.

Table I. Correlation of the stratification or contour with the shape of colorectal cancers.

| | Stratification (P=0.0196) | | Contour (P=0.4356) | | |
|---|---|---|---|---|---|
| Shape | Preserved | Lost | Smooth | Irregular | Total |
| W | 3 | 4 | 2 | 5 | 7 |
| M | 0 | 8 | 1 | 7 | 8 |
| Total | 3 | 12 | 2 | 12 | 15 |

The correlation was analyzed with the Chi-square test. W, wall thickening; M, mass.

*Correlation of stratification and contour with shape in CRC*. To determine whether there is an association between the shape of CRC and stratification or contour, Chi-square test was performed (Table I). Stratification was preserved in W, while it was lost in M (P=0.0196). The correlation between shape and contour was not significant (P=0.4356).

*Correlation of depth of invasion with shape, stratification and contour in CRC*. To analyze the association between the depth of invasion and the shape, stratification, or contour, Chi-square test was performed (Table II). No significant correlation was observed between any of the variables.

*Laboratory findings in colorectal cancer patients*. To assess the background of patients diagnosed with CRC using abdominal US, blood test variables were analyzed (Table III). The Hb level was below the normal range, whereas the CRP, CEA and CA 19-9 levels were above the normal range.

## Discussion

The threshold value of colonic wall thickness on abdominal US may be useful for the diagnosis of CRC. The upper limit of the normal colonic wall is 3 mm on CT (14).

Table II. Correlation of depth of invasion of colorectal cancer with shape, stratification and contour.

| Depth of invasion | W or M (P=0.1292) | | Stratification (P=0.1225) | | Contour (P=0.4686) | | Total |
|---|---|---|---|---|---|---|---|
| | W | M | Preserved | Lost | Smooth | Irregular | |
| MP | 1 | 0 | 1 | 0 | 0 | 1 | 1 |
| SS | 6 | 6 | 2 | 10 | 3 | 9 | 12 |
| SE | 0 | 2 | 0 | 2 | 0 | 2 | 2 |
| Total | 7 | 8 | 3 | 12 | 3 | 12 | 15 |

The correlations were analyzed with the Chi-square test. W, wall thickening; M, mass; MP, invasion of the muscularis propria; SS, invasion of the subserosa; SE, invasion beyond the serosa.

Table III. Laboratory findings in colorectal cancer patients.

| Findings | Range | Mean ± SD | Normal |
|---|---|---|---|
| WBC (x$10^3/\mu$l) | 3.1-19.0 | 8.0±4.5 | 3.5-8.5 |
| Hb (g/dl) | 3.9-14.7 | 10.8±5.3 | 11.5-15.0 |
| CRP (mg/dl) | 0.2-14.1 | 4.2±5.3 | 0-0.3 |
| CEA (ng/ml) | 1.5-44.2 | 18.9±17.9 | 0-5 |
| CA19-9 (U/ml) | 5.3-595 | 63.2±168 | 0-37 |

SD, standard deviation; WBC, white blood cell count; Hb, hemoglobin; CRP, C-reactive protein; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9.

Stermer *et al* performed colonoscopy in patients who had a wall thickened to >3 mm (15). Of the 46 patients, 30 had a wall thicker than 3 mm, but showed no abnormalities, suggesting that false-positive results may be found in patients with walls thicker than 3 mm; thus, the threshold value may be >3 mm. In our study, the thickness of normal colonic wall was <3 mm. Our data were consistent with previous results (15). A threshold value for colonic wall thickness has not been determined for the diagnosis of CRC. Our data clearly demonstrated a threshold value of 4.3 mm. The wall thickness in CRC has been reported to be 14 mm at the time of diagnosis with CT (16), suggesting that the threshold value of wall thickness for the diagnosis of CRC may be lower with abdominal US. This hypothesis may be supported by the fact that abdominal US provides more detailed findings compared with CT (11).

Loss of stratification is observed in 85% of patients with CRC (12). In our study, stratification was lost in patients with the M type of CRC. CRC is more advanced in the M type compared with the W type. Our data are supported by the fact that loss of stratification indicates CRC cell invasion (11). Regarding rectal cancer, endorectal US is suitable for the evaluation of the extent and staging of rectal cancer (17,18). However, endorectal US is not suitable for screening, in contrast to abdominal US. Moreover, our data clearly indicated that abdominal US was useful for the evaluation of the extent of CRC.

Our data demonstrated that the Hb level was lower and CRP was higher compared with the normal values in patients with CRC. It has been demonstrated that CRC is associated with bleeding and inflammation (19). An elevated CRP level indicates that CRC is advanced and the prognosis is poor (20). Lower Hb level is associated with Dukes' stages B and C, rather than with stage A (21). CEA and CA 19-9 are known markers of CRC (22). Our results demonstrated that the CEA and CA 19-9 levels were higher compared with the normal values. CEA correlates with disease-free survival after surgery for CRC (23). These results and previous reports suggest that CRC diagnosed with abdominal US is advanced.

The major limitation of our study was the small number of patients, as the enrolled patients were restricted to those diagnosed with CRC using abdominal US.

In conclusion, the threshold value of colonic wall thickness was 4.3 mm for the diagnosis of CRC with abdominal US. CRC was advanced at diagnosis, with higher CRP, CEA and CA 19-9 levels, and lower Hb levels.

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