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Original Article

Assessment of hepatic steatosis on contrast enhanced computed tomography in patients with colorectal cancer

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Abstract: Aims: Non-alcoholic fatty liver disease is often seen in patients with colorectal cancer. Insulin resistance and metabolic syndrome are related to increased risk of colorectal cancer. The aim of this study was to quantitatively determine the relationship between non-alcoholic fatty liver disease and colorectal cancer with the examination of routine abdominopelvic computed tomography images taken for staging. Methods: A retrospective evaluation was made of the colonoscopy and histopathology reports of 1630 patients who presented for a scanning or diagnostic colonoscopy examination. Colorectal cancer was determined histopathologically in 129 cases. Colorectal cancer patients with distant metastasis or additional malignancies were excluded from the study. A total of 105 patients met the criteria and were included in the study. A control group was formed of 94 patients with no history of cancer. The liver density on abdominopelvic computed tomography and serum transaminase values were recorded for the patients and compared with those of the control group. Results: The groups were similar in respect of age, gender and aspartate aminotransferase levels. Although not statistically significant, the alanine aminotransferase levels of the patient group were high compared to the control group. The liver density on computed tomography was statistically significantly lower in the patient group than in the control group. Conclusion: The liver density measurement on contrast abdominopelvic computed tomography of colorectal cancer patients was low, which is consistent with non-alcoholic fatty liver disease.

Keywords: Colorectal cancer, fatty liver, hepatosteatosis, computed tomography

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinical entity including simple fatty liver (SFL) and non-alcoholic steatohepatitis (NASH) which has been diagnosed more often in recent years [1]. SFL is a benign condition but NASH may lead to cirrhosis and hepatic adenocarcinoma [2]. NAFLD has been reported at a prevalence of 75% in obese patients and is thought to be a component of metabolic syndrome [3, 4]. There is a relationship between insulin resistance and metabolic syndrome and increased risk of colorectal cancer (CRC) [5]. Insulin and insulin growth factor play a role in the development of CRC with proliferative and antiapoptotic effects. In addition, adiponectin expression is reduced in patients with NAFLD and hypoadiponectinemia is related to increased CRC risk. By raising insulin resistance, hypoadiponectinemia leads to hyperinsulinemia and increased cell proliferation [5, 6]. In a study by Hwang et al, evaluating hepatic steatosis with ultrasonography (USG), a relationship was determined between colon adenomatous polyps and NAFLD [5]. Wong et al reported an increase in the incidence of advanced stage CRC and colon adenomatous polyps seen in NAFLD cases [7].

Liver biopsy is the gold standard in NAFLD diagnosis. However, as it is an invasive method, imaging methods to determine NAFLD are more

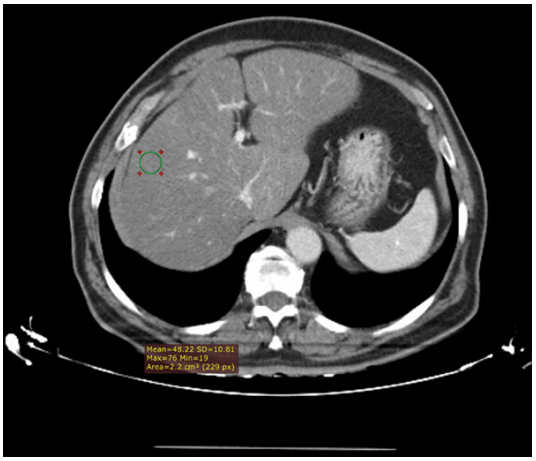

Figure 1. 46-year-old women with abnormal liver function tests. Axial contrast-enhanced CT image shows diffuse low attenuation of liver. Liver measured 48, 22 HU consistent with fatty infiltration of liver.

preferred. USG is the most widely used imaging method to determine hepatosteatosis, and it can also be evaluated by computed tomography (CT) and chemical shift magnetic resonance imaging (MRI). In the determination of steatosis, USG has been reported at rates of 60-94% sensitivity and 84-95% specificity. Chemical shift MRI sensitivity is 90% and specificity is 91% [8]. Park et al reported unenhanced CT sensitivity of 82% and specificity of 100% in the determination of hepatosteatosis [9]. Most CT imaging taken for staging purposes in routine practice is with contrast. In a study by Kim et al, contrast CT was shown to be more successful than non-contrast CT in the determination of hepatosteatosis in 179 liver donors [10]. Using non-contrast CT examination, Idilman et al determined increased NASH incidence in patients with Type 2 DM and coronary stenosis [11]. In the current study, liver density was evaluated on routinely taken contrast abdominopelvic CT images of cases diagnosed with CRC.

Methods

A retrospective examination was made of the colonoscopy reports and histopathological evaluation results of 1630 patients who underwent scanning or diagnostic colonoscopy between 2009 and 2014. In 129 cases, CRC was determined histopathologically. Colorectal cancer patients with distant metastasis or additional malignancies were excluded from the study. A total of 105 patients met the criteria and were included in the study. The abdominopelvic CT images performed for the purpose of staging were evaluated retrospectively. The images were taken on an abdominopelvic CT device (Toshıba Activion 16) and in the portal phase 100 mL of iohexol (Omnipaque 300, GE Healthcare) was administered to all patients. The portal phase images were obtained 45 seconds after contrast substance injection at 3 ml/sec using a pump. On the contrast CT image, the mean of Hounsfield unit (HU) density measurements taken from 3 different areas of the left and right lobes not including non-vascularised and calcification areas in a region of interest (ROI) 2 cm^2. The liver and other organs were re-evaluated in respect of metastasis.

The healthy control group comprised 95 individuals with no oncological or systemic disease and no history of diabetes mellitus, obesity or metabolic syndrome and who were not found to have fatty liver on contrast CT. Serum biochemical test results taken from the patients and control group at the time the CT images were performed were recorded from the digital archives.

The study was performed according to the guidelines of the Declaration of Helsinki, and it was approved by the ethics review committee of our hospital.

SPSS (Statistical Package for Social Science) 17.0 for Windows was used to analyze the data. Continuous variables were presented as mean ± standard deviation. Histograms and the One-Sample Kolmogorov-Smirnov Test were used to evaluate whether the continuous variables were distributed normally. The significance of the difference between the independent variables that were not normally distributed was evaluated with the Mann Whitney U test in two groups and Kruskall-Wallis test for more than two groups. The Pearson Test was used for correlation analysis of continuous variables. All statistical calculations were made two-tailed. A value of $p<0.05$ was considered statistically significant.

Results

The 105 cases with colorectal cancer were 65 males (61.9%) and 40 females (38.09%) with a mean age of 60.17±12 years. The CT scores were determined as 96.87±11.9 in the control

Table 1. Comparison between patient and control groups in respect of biochemical parameters and CT score

	Control	CRC	p[1]	CRC Subgroups			
				Right Colon	Transverse Colon	Left Colon	P[2]
Sex							
Male (n (%))	48 (51.1%)	65 (61.9%)	0.062	14 (66%)	20 (66.6%)	31 (62%)	0.658
Female (n (%))	46 (48.9%)	40 (38.1%)		11 (44%)	10 (33.3%)	19 (38%)	
Age (mean ± sd)	59.27±16.4	60.17±12.0	0.953	55.7±15.7	61.1±11.6	59.5±11.8	0.600
AST (mean ± sd)	26.17±13.2	28.77±18.0	0.568	35.1±15.5	25.3±13.7	33.1±24.0	0.073
ALT (mean ± sd)	22.07±22.9	22.57±13.1	0.062	23.4±12.2	20.7±16.5	23.9±33.5	0.478
CT score (mean ± sd)	96.87±11.9	68.70±18.7	<0.001	64.8±18.4	70.6±18.3	69.6±19.8	0.834

[1]*P* value of comparison of control and CRC group. [2]*P* value of comparison of CRC subgroups.

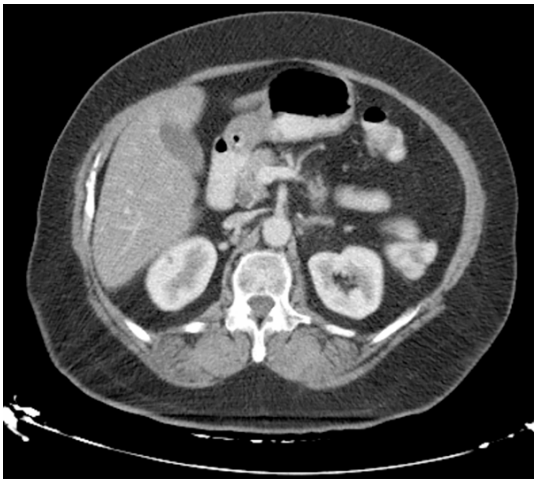

Figure 2. Axial contrast-enhanced CT image shows area of increased attenuation along gallbladder fossa, consistent with focal fatty sparing.

group and 68.70±18.7 in the patient group (**Figure 1**). Age, gender and AST values were found to be similar in both groups. Although the ALT values were higher in the patient group, there was no statistical significance. The CT score of the control group was found to be statistically significantly higher than that of the patient group. In the patient group, when comparison was made of subgroups according to the location of the cancer, there was no statistically significant difference in the CT score (**Table 1**).

In 21 patients (20%) of the CRC patient group, non-fatty areas were determined in the anterior of the portal vein (n=15, 71.4%) and adjacent to the gallbladder (n=6, 28.6%) (**Figure 2**). When the patients of the CRC patient group determined with non-fatty areas were compared with the CRC patient group not determined with non-fatty areas, the CT scores were similar (65.9±10.5 and 69.4±18.7, p=0.14).

Discussion

In the examination of contrast abdomen CT of CRC cases, liver densities indicating steatosis were determined to be significantly low. Other conditions which may cause diffuse low levels in liver density are diffuse malignant infiltration and amyloid infiltration.

Evaluation of hepatosteatosis is generally made with non-contrast CT. In daily practice, contrast images are preferred in routine abdomen CT evaluations. In the current study, the fatty status of the liver was evaluated on contrast CT images performed for the staging of CRC patients and there was not felt to be any need for any additional examination. In the evaluation of hepatic steatosis, contrast and non-contrast images have close rates of accuracy [10]. Lawrence et al determined sensitivity of 60% and specificity of 100% in contrast CT in a qualitative evaluation determining focal non-fatty areas in the determination of hepatosteatosis [12]. In a study comparing liver and spleen densities on contrast CT, Johnston et al reported that contrast CT showed sensitivity of 54-71% in the evaluation of hepatosteatosis [13]. In the current study, the CT scores were similar in patients of the CRC patient group determined with non-fatty areas to those of the CRC patient group not determined with non-fatty areas, thus indirectly indicating the presence of non-fatty areas in hepatosteatosis and therefore the CT scores obtained in the CRC patient group were thought to be consistent

with NAFLD. Several studies have reported a relationship between CRC and hepatosteatosis. In a study by Lin et al of an extensive group of 2315 patients, very high rates of CRC were determined in NAFLD patients and it was reported that NAFLD could be an independent risk factor in CRC [14].

Stadlmayr et al applied colonoscopy screening to 1211 cases evaluated with USG in respect of fatty liver and it was determined that of 632 cases with NAFLD, 53.3% had colon adenomatous polyps and 1% had CRC. From these results obtained with USG, Stadlymayr et al recommended colonoscopy for scanning purposes in cases determined with steatosis in the liver [15].

Determination before hepatosteatosis is important in CRC cases in respect of differentiation from hepatopathies which develop associated with chemotherapy [16, 17]. Miyake et al showed that 5-Fluorouracil and UFT in CRC patients increased hepatic steatosis [16]. In the current study, the data of the CRC patients at the time of diagnosis were evaluated. Advanced stage CRC is generally seen as lipolysis with the effect of tumour necrosis factor (TNF). Therefore in advanced stage tumours, accumulation of fat in the liver is not an expected event. In a study by Murono et al of 604 CRC patients, hepatosteatosis was determined with non-contrast CT in CRC patients and a lower rate of metastasis to the liver was seen in CRC patients without hepatosteatosis [18]. In the current study, all the cases were CRC patients with no distant metastasis as the tumour was limited to the colon.

The density measurements on contrast CT of CRC patients suggest a higher rate of hepatosteatosis in CRC patients. These findings are consistent with those in literature. CRC patients can be evaluated for hepatosteatosis by making liver HU measurement with contrast abdominopelvic CT without the need for any additional examination. Hepatosteatosis can be evaluated on contrast abdominal CT images which are often taken for various indications in daily practice. For patients determined with low liver HU values on abdominopelvic CT, further evaluation may be necessary in respect of CRC.

Disclosure of conflict of interest

None.

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