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The Relationship between Colorectal Cancer and Abdominal Adipose Tissue Distribution

Kolorektal Kanser ve Abdominal Yağ Doku Dağılımı Arasındaki İlişki

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Abstract

Aim: To examine the relationship between obesity and the subcutaneous, visceral and retroperitoneal adipose tissue thicknesses of the abdomen.

Material and Method: The study included 62 control and 68 colorectal cancer patients. Abdominal computed tomography of the patients, which were taken within the last 6 months before preoperative or colonoscopic examination were evaluated. Colorectal cancer patients were divided into two groups as proximal and distal according to tumor localization. Subcutaneous, visceral and retroperitoneal adipose tissue thicknesses of the abdomen were measured using abdominal computed tomography scans.

Results: There was no statistically significant difference between the colorectal cancer group and the control group in terms of body mass index, retroperitoneal and visceral adipose tissue thickness and gender (p=0.091; 0.246; 0.531; 0.190,respectively). The mean age of the colorectal cancer group was higher (p<0.001). The mean subcutaneous adipose tissue thickness of the control group was higher (p=0.045). There was no statistically significant difference between the proximal and distal colorectal cancer group in terms of age, retroperitoneal, subcutaneous and visceral adipose tissue thickness (p=0.734; 0.916; 0.800; 0.170, respectively). The mean body mass index of the group with distal mass was higher (p=0.028). The proportion of males was higher in the group with distal mass than in the group with proximal mass (p=0.024).

Conclusion: In the risky population evaluating the adipose tissue in the abdomen and its distribution before the colorectal cancer is diagnosed or the symptoms develop will indicate which patients should be followed up in more detail and help to prevent more cases of colorectal cancer.

Keywords: Computed tomography; colorectal cancer; visceral adipose tissue; abdominal subcutaneous adipose tissue; retroperitoneal adipose tissue

Öz

Amaç: Abdominal subkütan, viseral ve retroperitoneal yağ dokusu kalınlıkları ile obezite arasındaki ilişkiyi incelemek.

Gereç ve Yöntem: Çalışmaya 62 kontrol ve 68 kolorektal kanser hastası dahil edildi. Hastaların ameliyat öncesi veya kolonoskopik muayenesinden önceki son 6 ay içinde çekilen abdominal bilgisayarlı tomografi tetkikleri değerlendirildi. Kolorektal kanser hastaları tümör lokalizasyonuna göre proksimal ve distal olarak iki gruba ayrıldı. Abdomenin subkütan, viseral ve retroperitoneal yağ doku kalınlıkları abdominal bilgisayarlı tomografi tetkikleri kullanılarak ölçüldü.

Bulgular: Kolorektal kanser grubu ile kontrol grubu arasında vücut kitle indeksi, retroperitoneal ve viseral yağ doku kalınlığı ve cinsiyet açısından istatistiksel olarak anlamlı bir fark yoktu (sırasıyla p=0.091; 0.246; 0.531; 0.190). Kolorektal kanser grubunun yaş ortalaması daha yüksekti (p <0.001). Kontrol grubunun ortalama subkütan yağ doku kalınlığı daha yüksekti (p=0.045). Proksimal ve distal kolorektal kanser grubu arasında yaş, retroperitoneal, subkütan ve viseral yağ doku kalınlığı açısından istatistiksel olarak anlamlı bir fark yoktu (sırasıyla p=0.734; 0.916; 0.800; 0.170). Distal kitle olan grubun ortalama vücut kitle indeksi daha yüksekti (p=0.028). Distal kitle olan grupta erkeklerin oranı proksimal kitlesi olan gruba göre daha yüksekti (p=0,024).

Sonuç: Riskli popülasyonda kolorektal kanser teşhisi konmadan veya semptomlar gelişmeden önce abdomendeki yağ dokusunu ve dağılımını değerlendirmek, hangi hastaların daha detaylı izlenmesi gerektiğini gösterecek ve daha fazla kolorektal kanser vakasının oluşumunu önlemeye yardımcı olacaktır.

Anahtar Kelimeler: Bilgisayarlı tomografi; kolorektal kanser; viseral yağ dokusu; abdominal subkütan yağ dokusu; retroperitoneal yağ dokusu

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INTRODUCTION

Colorectal cancer is the 3rd most common cancer in the world and is one of the leading causes of cancer-related deaths, especially in western countries. In developing countries, its incidence has been increasing in the last few decades. Obesity, high-fat/low-fiber diet, smoking and inadequate physical activity are among the important risk factors for the development of colorectal cancer.[1] In particular, the prevalence of obesity has increased significantly in the last thirty years and is considered an important risk factor for various types of cancer, including colorectal cancer.[2]

Until now, many epidemiological studies have been conducted investigating the relationship between the risk of colorectal cancer development and obesity, and it has been shown that there is a relationship between body mass index (BMI), waist circumference and waist/hip ratios and colorectal cancer.[3,4] However, the relationship between obesity and colorectal cancer is controversial. Unlike general obesity and BMI, it has been reported that body fat distribution, especially abdominal obesity, plays a more important role in the development of colorectal cancer.[5,6] BMI is not an exact measurement and may not take into account body fat composition and distribution. Abdominal adipose tissue (AT) can be roughly divided into 2 main compartments as visceral and subcutaneous AT. The visceral compartment can also be divided into two regions as peritoneal and retroperitoneal. Due to the individual differences in abdominal AT distribution, these compartments should be investigated separately to evaluate obesity more accurately.[7,8]

Computed tomography (CT) is one of the most accurate radiological methods for evaluating abdominal AT and has the ability to accurately measure abdominal AT distribution.[9] There are many studies on visceral fat area (VFA), especially in patients with colorectal cancer. In these studies, it has been shown that VFA is positively associated with colorectal cancer.[10-12] Nevertheless VFA measurement is not a routine procedure and requires special evaluation, time and technical equipment.

In the literature, there are also studies investigating the association between cancerous and cardio-metabolic diseases and obesity by measuring AT thickness in the abdominal cavity, which is a more practical method than fat area or volume measurements.[13-15] Especially in the literature, there are studies specifically investigating the effect of retroperitoneal AT on metabolic syndrome in different clinical situations. Studies have shown that retroperitoneal AT is more biologically active and the amount of AT is important for carcinogenic, cardiometabolic diseases and metabolic syndromes.[13,16,17] Therefore in this study we aimed to examine the relationship between obesity and the thicknesses of the AT in different compartments of abdomen, especially retroperitoneal region, since this was studied very little before.

MATERIAL AND METHOD

This retrospective study included 62 normal patients (control group) who were found to have no cancer by colonoscopy and 68 colorectal cancer patients who were histopathologically diagnosed between January 2015 and December 2018. The Institutional Review Board approved the study protocol. Among patients with colorectal cancer; patients with recurrent colorectal cancer, limited or palliative resection patients, patients who had previous intra-abdominal cancer surgery or emergency surgery for tumor-related complications, patients who had major surgery which can affect the amount of abdominal AT, patients who received neoadjuvan chemotherapy and those who were diagnosed with adenomatous popliposis were excluded from the study. The control group consisted of patients whose colonoscopy was reported as normal and who had an abdominal CT performed within the last 6 months prior to colonoscopy. In the control group, patients with a history of major abdominal surgery, patients who underwent surgery affecting the amount of abdominal AT, and patients diagnosed with any cancer in the present abdominal CT were excluded from the study. A total of 130 patients were included in the study, 47 of them were women and 83 were men. Age, gender, height and weight values of the patients were recorded. BMI was calculated as BMI=weight/(height)^2. Abdominal CT scans of colorectal cancer patients, which were taken within the last 6 months before preoperative or colonoscopic examination, were evaluated. Tumor localizations were determined by examining the abdominal CT of the patients. Colorectal cancer patients were divided into two groups as proximal and distal according to tumor localization. The cecum, ascending colon, and transverse colon were considered in the proximal group, while the distal group included splenic flexure, descending colon, sigmoid colon and rectum.[8] Patients were categorized as early-stage (stages 1-2) and advanced-stage (stages 3-4).

Abdominal CT was performed using a 128-slice CT scanner (General Electric Optima CT 660) and the following parameters: voltage: 120 kV; tube current: 100-400 mA; gantry rotation: 0.6 s; detector coverage: 40 mm; helical thickness: 5 mm; pitch and speed: 1.531 mm and 61.25 rotation, respectively. CT image data were evaluated using a GE Advantage Workstation (GE Healthcare, Buc, France) with Volume Share 7 software version. All distance measurements were made by the same radiologist experienced in abdominal evaluation.

Abdominal CT images of the colorectal cancer and control groups were obtained from the picture archiving and communication system of our hospital. Abdominal CT images in axial section at the soft tissue window were used. Abdominal AT thicknesses taken from 3 different regions were measured and noted. Retroperitoneal AT; it was obtained by measuring the distance between the left kidney and the posterior abdominal wall at the level of the left renal vein.[13] Visceral AT; the distance from the anterior abdominal wall

to the vertebra was measured at the level of the umbilicus. Abdominal subcutaneous AT; the distance between the left rectus muscle and the skin was measured at the umbilicus level (**Figure**).

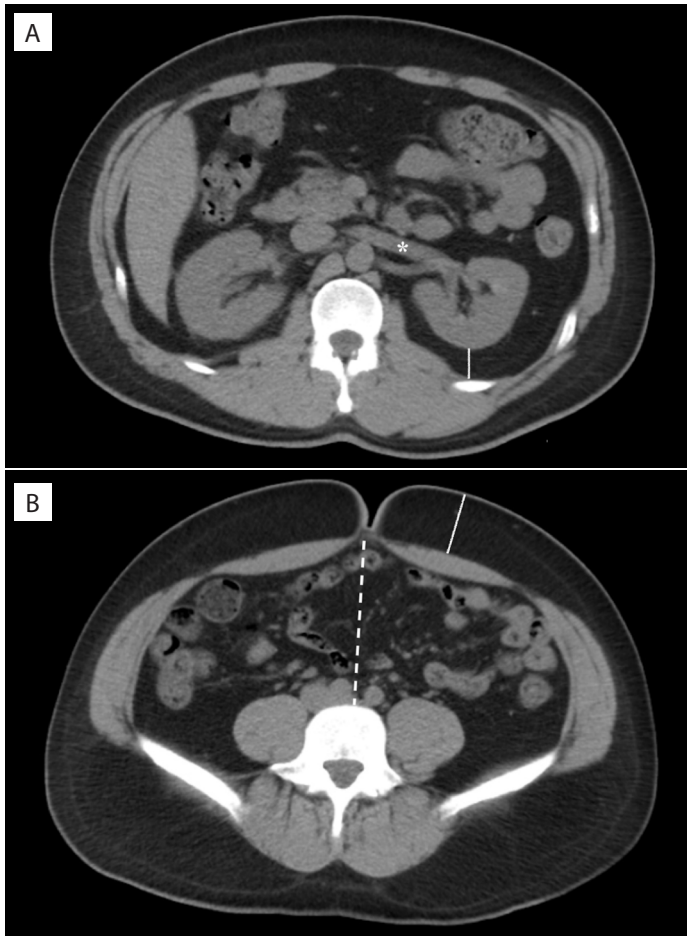

Figure. Measurement of adipose tissue thickness on axial CT slices **A.** Retroperitoneal adipose tissue: measured using the vertical distance between the left posterior renal capsule and the posterior abdominal wall at the level of the left renal vein (*). **B.** Visceral adipose tissue: measured as the distance from the anterior abdominal wall to the vertebra at the level of the umbilicus (dashed line); Abdominal subcutaneous adipose tissue: measured as the distance between the left rectus muscle and the skin at the umbilicus level (straight line).

Statistical Analysis

In our study, the 21.0 version of the SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) program was used for the statistical analysis of the data. Mean value, standard deviation, median, minimum and maximum values for continuous variables in descriptive statistics; number and percentage values were calculated for discrete variables. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate the normal distribution as initial analyzes. For comparisons between groups, Mann Whitney U, chi-square test was used for nonparametric data, and independent groups t test was used for parametric data. Results were evaluated at 95% confidence interval and $p < 0.05$ was defined as statistical significance.

RESULTS

A total of 130 cases were included in this study. 68 patients were diagnosed with colorectal cancer and 62 were control group. 83 (63.8%) of the patients were male and 47 (36.2%) were female. In the colorectal cancer group of the 68 patients, 47 (69.1%) were male and 21 (30.9%) were female. Thirty-eight (55.9%) patients have mass in the proximal location and 30 (44.1%) in the distal location. Fifty-six (82.4%) of the colorectal cancer patients were in the advanced stage, while 12 (17.6%) were in the early stage. Twenty-two (57.9%) of those with proximal mass were men and 16 (42.1%) were women. Of the distal masses, 25 (83.3%) were male and 5 (16.7%) were female. The control group consisted of 36 (58.1%) men and 26 (41.9%) women. Mean ages; total group, those with colorectal cancer, those with proximal mass, distal mass, and control groups, respectively, 62.08±14.14 (27-88) years, 66.37±12.11 (33-88) years, 66.82±13.11 (33-87) years, 65.80±10.88 (42-88) and 57.37±14.79 (27-84) years (**Table 1**).

There was no statistically significant difference between the colorectal cancer group and the control group in terms of BMI, retroperitoneal and visceral AT thickness and gender (respectively p=0.091; 0.246; 0.531; 0.190). When the two groups were compared in terms of age, a statistically significant difference was found, and it was observed that the mean age of the colorectal cancer group was higher ($p<0.001$). When the two groups were compared in terms of abdominal subcutaneous AT thickness, a statistically significant difference was found, and the mean of the control group was higher (p=0.045) (**Table 1**).

When 68 cases with colorectal cancer were compared in terms of localization of the mass, no statistically significant difference was found in terms of age, retroperitoneal, subcutaneous and visceral AT thickness (p=0.734; 0.916; 0.800; 0.170, respectively). When these two groups were compared in terms of BMI, a statistically significant difference was found, and the mean BMI of the group with distal mass was higher (p=0.028). When these two groups were compared in terms of gender, a statistically significant difference was found, and it was observed that the proportion of males was higher in the group with distal mass than in the group with proximal mass (p=0.024) (**Table 2**).

DISCUSSION

In the present study, no statistically significant difference was found between the group with colorectal cancer and the control group in terms of BMI, retroperitoneal and visceral AT thickness and gender. Abdominal subcutaneous AT thickness was significantly higher in the control group compared with the colorectal cancer group. The BMI values of the distal colorectal cancer group were significantly higher than the group with proximal mass.

Table 1. Demographic characteristics of study groups.

	Total Mean±SD	Colorectal cancer group (n=68)	Control group (n=62)	p-value
Age	62.08±14.14	66.37±12.11	57.37±14.79	<0.001
BMI	27.58±4.87	26.88±4.86	28.28 (4.81)	0.091*
Retroperitoneal AT	14.65±8.56	15.71±9.60	13.50±7.17	0.246*
Subcutaneous AT	22.33±8.82	20.96±7.45	23.84 ±9.96	0.045*
Visceral AT	103.38±30.39	104.99±32.34	101.63±28.25	0.531
Male (%)	83 (63.8)	47 (69.1)	36 (58.1)	0.190**
Female (%)	47 (36.2)	21 (30.9)	26 (41.9)	

*Mann-Whitney U test ** Chi-square test p<0.05
BMI body mass index, Retroperitoneal AT retroperitoneal adipose tissue, Subcutaneous AT subcutaneous adipose tissue, Visceral AT visceral adipose tissue

Table 2. Relationship of study parameters with colorectal cancer localization.

	Distal mass (n=30) Mean±SD	Proximal mass (n=38) Mean±SD	p-value
Age	65.80±10.88	66.82±13.11	0.734
BMI	28.36±5.17	25.63±4.27	0.028
Retroperitoneal AT	16.77±12.23	14.87±6.93	0.916*
Subcutaneous AT	21.20±7.74	20.76±7.32	0.800*
Visceral AT	111.07±31.75	100.18±32.40	0.170
Male (%)	25 (83.3)	22 (57.9)	0.024**
Female (%)	5 (16.7)	16 (42.1)	

*Mann-Whitney U test ** Chi-square test p<0.05
BMI body mass index, Retroperitoneal AT retroperitoneal adipose tissue, Subcutaneous AT subcutaneous adipose tissue, Visceral AT visceral adipose tissue

Obesity, which is becoming widespread throughout the world, creates a huge burden on the health system and increases the incidence of various chronic diseases and cancer, especially colorectal cancer.[18,19] Epidemiological data show that obesity increases the risk of colorectal cancer by 30-70%, especially in men.[3] BMI is mostly used in the assessment of obesity in daily practice. Distribution of AT in the body rather than general adiposity may be more directly related to the risk of developing colorecral cancer.[11] A normal BMI can mask potentially dangerous fat in the presence of low muscle mass.[20] Variable body composition in different races, various physical factors (gender, age, diet, hormone, medication) may vary the distribution of AT in obese patients. Therefore, BMI may not give accurate results regarding body fat distribution.[21] In addition to anthropometric measurements such as waist circumference, waist-to-hip ratio, and waist-to-height ratio; three-dimensional body scanning, dual abdominal bioelectric impedance analysis, ultrasound, dual-energy X-ray absorptiometry, and cross-sectional imaging methods such as CT and MRI are the methods used for the evaluation of obesity, especially abdominal obesity. CT and MRI provide detailed observation of the anatomy due to their ability to provide multidimensional examination, and thus they are seen as reference methods for abdominal AT measurement.[9] In the literature there are studies investigating the relationship between obesity and colorectal cancer and colorectal cancer outcome. In these studies, different results were found depending on the method used or the selected patient populations and their different clinical characteristics.[5,10-12,22-25] Lee et al.[12] found that VFA is positively associated with the prevalence of colorectal cancer. Although they could not comment on causality, they stated that visceral fat may be associated with the risk of colorectal cancer. Seo et al.[8] found that VFA measured by CT scan was positively associated with the presence of colorectal adenoma, especially in men. Im et al.[26] found that higher VFA was dose-dependently associated with a higher risk of incident adenoma. Oh et al.[11] reported that increased VAT is an independent risk factor for colorectal cancer. Yamamoto et al.[10] concluded that visceral AT accumulation may promote the development of early-stage cancer in the colorectum. Akay et al.[23] found statistically significant lower VAT and SAT volumes in patients with early-stage colorectal cancer compared with the control group. Erarslan et al.[22] found that VFA was not associated with colorectal adenoma and carcinoma. Choe et al.[27] showed that visceral obesity is not a risk factor for early colorectal cancer.

In general abdominal AT is located in two main compartments, visceral and subcutaneous, and the main metabolically active part is the visceral one. More specifically, in the abdominal cavity there are omental, mesenteric and retroperitoneal AT compartments. Omental and mesenteric AT together can be referred to as the peritoneal compartment. Leitner et al.[28] showed that activated brown AT was not found in either the subcutaneous or peritoneal compartment, was found predominantly in the perirenal and pararenal AT. The drainage of the peritoneal and retroperitoneal regions is different, as well as the composition and amount of adipokines released from these regions.[16] For such reasons peritoneal and retroperitoneal AT may play different roles in our metabolism. Based on this idea, we wanted to investigate not only the relationship between visceral and subcutaneous AT and colorectal cancer but we also specifically wanted to investigate the relationship between the more biologically active retroperitoneal AT and colorectal cancer. When we look at the studies investigating

the relationship between colorectal cancer and obesity in the literature, we see that there is no separation of retroperitoneal AT in VFA and volume measurements used in AT evaluation. We aimed to measure subcutaneous, visceral and retroperitoneal AT thicknesses instead of fat area or volume measurement in abdominal CT as it would be more practical and accessible in daily practice. In addition, retroperitoneal AT measurement can be performed more objectively with thickness measurement. Also we think that measuring AT thickness will be a more accurate approach since there may be inaccurate measurements due to the movements of the bowels in the sections taken in the VFA measurement.

In this study no statistically significant difference was found between the colorectal cancer and the control group in terms of BMI, retroperitoneal and visceral AT thickness. Most of the patients diagnosed with colorectal cancer were diagnosed at an advanced stage, so we believe that cancer related cachexia may have affected the amount of visceral, subcutaneous and retroperitoneal AT thicknesses. Also the reason why subcutaneous AT is more in the control group can also be explained in the same way. Although Mahamid et al.[13] did not comment on this issue, they found that lean patients tended to have more advanced stages than patients with greater retroperitoneal AT thickness may be attributed to the same reason. Therefore, it is necessary to evaluate the amount and distribution of abdominal AT in the risky population before developing colorectal cancer. Song et al.[29] 's study found that an increase in waist circumference in adulthood may be associated with a higher risk of colorectal cancer in men. In addition, they emphasized the importance of having a healthy waist for the prevention of colorectal cancer.

While proximal colon cancers present with mild findings and systemic symptoms such as anemia and weight loss, those located distally present with changes in bowel movements and rectal bleeding.[30] Therefore, distal colon cancers present faster than proximal ones. In the study, the BMI of the group with a distal mass was found to be significantly higher than the group with a proximal mass, because of the earlier findings in cases with a distal mass among colon cancer patients. Patients with distal mass compared to those with proximal mass can be diagnosed before cancer-related weight loss becomes evident.

There are several limitations in this study. The low number of patients caught at an early stage among the patients who achieved colonoscopy and CT examination in this retrospective study can be considered as the major limitation of this study. This study should be conducted in a larger population consisting of early stage patients. To obtain early stage patients, a population consisting of screening patients can be used. But this study could not be designed prospectively, as the use of CT in an asymptomatic screening population due to radiation exposure may raise ethical questions in our country. Therefore, in this study, we used CT scans that were previously performed for various reasons in the control group or required for preoperative evaluation in colorectal cancer patients. Another limitation of this study is that it is not known how long patients have had colorectal cancer. Because the duration of the disease will affect the amount of abdominal AT.

CONCLUSION

The present study's findings show that there was no relationship between colorectal cancer and retroperitoneal and visceral AT thicknesses in diagnosed colorectal cancer patients. While the relationship between obesity and colorectal cancer is known, this result emphasizes the importance of evaluating the abdominal AT amount and its distribution in the abdominal cavity before the diagnosis of cancer or the development of symptoms. Thus, information can be obtained about patients who need to be followed up in more detail in the risky population. Further studies should be planned to compare retroperitoneal AT and visceral AT, including a larger patient population with early stage patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: Fatih Sultan Mehmet Training and Research Hospital's Institutional Review Board approved this study protocol (Approval Date: 21.02.2020, Decision Number: 3304).

Informed Consent: Informed consent for Computed Tomography has been obtained from the patients who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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