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***Original Article** / Özgün Makale*

The comparison of wall thickness of esophagus and gastroesophageal junction using computed tomography with endoscopy and biopsy results

Bilgisayarlı tomografi kullanılarak özofagus ve gastroözofageal bileşke duvar kalınlığının endoskopi ve biyopsi sonuçları ile karşılaştırılması

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ABSTRACT

Background: This study aims to establish a cut-off value for increases in the esophageal wall thickness measured using computed tomography to differentiate between benign and malignant pathologies.

Methods: A total of 144 patients (61 males, 83 females; mean age 57.2±12.4 years; range, 24 to 86 years) who underwent thoracic and/or abdominal computed tomography in the radiology clinic between January 2015 and June 2018 for any reason and who were found to have a thickening of the esophageal wall or gastroesophageal junction were retrospectively analyzed. Tomography images were examined by two radiologists who reached consensus on the wall morphology and thickness, anatomic localization, and any accompanying findings regardless of the endoscopy results. Benign and malignant patients were identified from the endoscopy and/or biopsy results. The receiver operating characteristic analysis was carried out to establish a cut-off value for the lesion wall thickness to differentiate between benign and malignant pathologies and to determine a cut-off value for the lesion-level thickness-normal segment thickness ratio.

Results: A statistically significant difference was found in the wall thicknesses of patients with esophageal cancer and those with benign lesions. According to a cut-off value for wall thickness of 13.5 mm, sensitivity and specificity were found to be 94.3% and 100%, respectively. The lesion-level thickness-normal segment thickness ratio was found to be statistically significant in malignant-benign differentiation, and a significant correlation was found between the asymmetric thickening and malignancy.

Conclusion: Increases in the esophageal wall thickness and asymmetry detected on computed tomography can contribute to the early diagnosis of esophageal cancers, particularly in regions endemic to esophageal cancer as in Van province in eastern anatolia region of Turkey. Asymmetric wall thicknesses over 13.5 mm would be highly significant in terms of malignancy in tomographic examinations.

Keywords: Computed tomography, esophageal cancer, thickness of esophageal wall.

ÖZ

Amaç: Bu çalışmada, benign ve malign patolojilerin ayırt edilmesi amacıyla bilgisayarlı tomografide ölçülen özofagus duvar kalınlığındaki artışlar için bir eşik değeri oluşturmak amaçlanmıştır.

Çalışma planı: Ocak 2015 - Haziran 2018 tarihleri arasında radyoloji kliniğinde herhangi bir nedenle toraks veya batın bilgisayarlı tomografisi çekilen ve özofagus duvar veya gastroözofageal bileşkede kalınlık tespit edilen 144 hasta (61 erkek, 83 kadın; ort. yaş 57.2±12.4 yıl; dağılım, 24-86 yıl) retrospektif olarak incelendi. Tomografi görüntüleri iki radyolog tarafından, endoskopi veya biyopsi sonuçlarından bağımsız olarak, duvar morfolojisi ve kalınlığı, anatomik lokalizasyonu ve eşlik eden bulgular açısından görüş birliğine varılarak incelendi. Endoskopi veya biyopsi sonuçlarına göre benign ve malign hastalar belirlendi. Lezyon duvar kalınlıkları ile benign ve malign patolojilerin ayrımında eşik değer belirlemek için ve lezyon düzeyindeki kalınlığın normal segment kalınlığına oranının eşik değerini belirlemek için alıcı işletim karakteristik analizi yapıldı.

Bulgular: Özofagus kanserli hastalar ve benign lezyonlu olanların duvar kalınlığında istatistiksel olarak anlamlı bir fark saptandı. Duvar kalınlığı için 13.5 mm'lik eşik değerine göre, duyarlılık ve özgüllük sırasıyla %94.3 ve %100 olarak bulundu. Lezyon düzeyindeki kalınlığın normal segment kalınlığına oranı, malign-benign ayrımında istatistiksel olarak anlamlı saptandı ve asimetrik kalınlaşma ile malignite arasında anlamlı bir ilişki bulundu.

Sonuç: Özofagus duvar kalınlığı ve bilgisayarlı tomografide saptanan asimetri artışı, özellikle Türkiye'nin doğu anadolu bölgesinde Van ili gibi özofagus kanserine endemik bölgelerde özofagus kanserlerinin erken tanısına katkıda bulunabilir. Tomografik incelemelerde 13.5 mm'nin üzerindeki asimetrik duvar kalınlıklarının malignite açısından oldukça anlamlı olacağı kanısındayız.

Anahtar sözcükler: Bilgisayarlı tomografi, özofagus kanseri, özofageal duvar kalınlaşması.

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Among the gastroesophageal tract malignancies, esophageal cancer is a disease with late-manifesting symptoms which spreads rapidly along the tract, often resulting in late referrals to the physician. According to 2012 data of the International Agency for Research on Cancer (IARC), esophageal cancer is the ninth leading cause of cancer-related death in women and the sixth in men worldwide.[1]

Squamous cell carcinoma (SCC) and adenocarcinoma are the most common primary esophageal malignancies with an etiology linked to tobacco and alcohol use, dietary habits (i.e., food containing nitrosamine, hot tea, diets lacking fresh vegetables), and obesity. Risk factors for esophageal SCC include Plummer-Vinson syndrome, achalasia, caustic esophagitis, tylosis, gluten enteropathy, and ionized radiation exposure.[2-5]

The incidence of esophageal cancer varies highly between different geographical regions in the world, and even between residential districts in close proximity within the same geographical region.[6,7] The region, defined as the esophageal cancer zone, in which SCC is particularly common, covers the area from northern China to the Middle East. The prevalence of esophageal cancer is 20 to 30 times more common in China than the United States.[8] Turkey and, particularly the eastern Anatolian region including Van province, falls within the esophageal cancer zone.[9]

Esophagoscopy is the most common means of identification of esophageal cancers, playing an important role not only in the diagnosis, but also in determining the upper and lower margins of the lesion. Computed tomography (CT) is the most helpful examination approach for the detection of extraesophageal invasion and metastases of the tumor. Endoscopic ultrasonography, on the other hand, may detect the penetration level of malignant lesions, the infiltration of adjacent organs and structures, and metastases to the regional lymph nodes, thereby leading to accurate tumor grading and the determination of appropriate treatment.[10] Positron emission tomography is another method used widely for staging in recent years. It is also available in studies with cine MRI in terms of invasion assessment.[11,12]

In the literature, there are many studies investigating the correlation between stomach, small intestine, and colon wall thickening detected on CT performed for any reason with biopsy results; however, the number of studies on esophagus is limited.[13,14] In the present study, therefore, we aimed to compare the wall thickness of esophagus and gastroesophageal junction (GEJ) using CT versus endoscopy and/or biopsy results and to establish a cut-off value for esophageal wall thicknesses detected on CT as a means of differentiating between benign and malignant pathologies.

PATIENTS AND METHODS

In this retrospective study, a total of 1,350 patients who underwent thoracic and/or abdominal CT in the radiology clinic between January 2015 and June 2018 for any reason and who were found to have a thickening of the esophageal wall or GEJ were initially screened. Among these patients, those who had an upper gastrointestinal system endoscopy and/or biopsy at the time of CT and within the previous and following month were evaluated. Patients with uncertain esophageal thickening or those whose single wall thickness could not be distinguished, and more than one month between the endoscopy and CT and artifact images were excluded from the study. The contrast material was administered intravenously (IV) in most of the patients; however, those who were not administered an IV contrast agent and who had a clearly detected thickening of the esophageal wall were included in the study. Finally, the study included a total of 144 patients (61 males, 83 females; mean age 57.2±12.4 years; range, 24 to 86 years) who met the inclusion criteria. An endoscopic diagnosis was established in 75 patients without the need for a biopsy after being considered benign based on clinical and radiological findings and the absence of mucosal irregularity by an endoscopist, and 69 patients were diagnosed pathologically after undergoing a biopsy from the suspected areas. A written informed consent was obtained from each patient. The study protocol was approved by the Van Yüzüncü Yıl University Faculty of Medicine Ethics Committee (Date: 03/08/2018; No. 03). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Imaging

All patients underwent thoracic and/or abdominal CT examinations in accordance with the prespecified protocol based on the preliminary diagnosis made by the radiology department. Patients who underwent an abdominal CT and an abdominal-thoracic CT at the same time were examined after 12 hours of fasting. Prior to the examination, the patients were asked to consume 1,000 to 1,500 mL of water (without contrast) within 1 h, drinking two cups (200 to 300 mL) of water every 10 min. The CT images were taken using a 16-slice multidetector CT (MDCT) device (Somatom Emotion 16-slice; CT2012E- Siemens AG, Berlin and Munich, Germany). For the contrast-enhanced

examinations, the patients were administered 100 mL of a non-ionized IV contrast agent iohexol (Omnipaque™; GE Healthcare Ireland, Cork, Ireland) or iopromide 300 (Ultravist 300, Bayer-Schering Pharma, Berlin, Germany) through a forearm vein at 3 mL/sec via an automatic injector (CT 9000 ADV Liebel-Flarsheim Company, Cincinnati, OH, USA). For the thoracic CT studies, cross-sections were obtained starting from the distal neck toward the upper abdomen. The patients with a preliminary diagnosis of a vascular pathology were asked to hold their breath for 25 sec following the administration of the contrast agent, and after 70 sec for other patients. For the abdominal CT examination, images were obtained from the diaphragm level to the symphysis pubis level after 70 sec following the administration of the contrast agent.

Radiological assessment

The data transferred to the system following the image-shooting procedures were re-analyzed in terms of esophageal and GEJ thickness. The axial and multiplanar reformatted images with 3-mm cross-sectional thickness were obtained using a 16-slice device and were evaluated by two radiologists with five and 18 years of experience, respectively, in the use of the high-resolution gray-scale medical monitors for routine CT examinations, based on a consensus and regardless of endoscopy results. The two radiologists assessed the images for wall morphology and thickness, anatomic localization, and accompanying findings (Figures 1-8). The wall thickness was measured on the axial plane from a single wall at the thickest esophageal area. Anatomical localization was determined as cervical, upper thoracic, middle thoracic, and lower thoracic esophagus in line with the 7th edition of the Tumor, Node, Metastasis (TNM) classification system. Gastroesophageal cancer was defined as a malignancy with a tumor centered in the lower thoracic-esophagus, located 5-cm proximal to the GEJ or stomach, and with invasion of the junction or the distal thoracic

Figure 2. A 61-year-old female patient, asymmetric thickening measured as 12.4 mm in the gastroesophageal junction with a biopsy result of an adenocarcinoma.

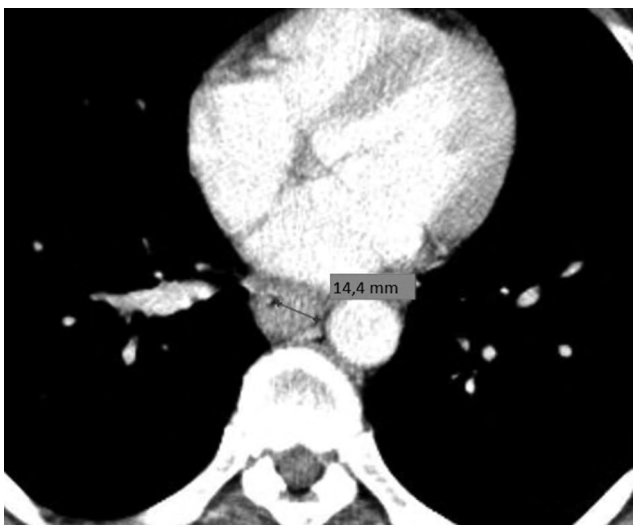

Figure 1. A 62-year-old male patient, asymmetric thickening measured as 14.4 mm in the middle thoracic esophagus with a biopsy result of squamous cell carcinoma.

Figure 3. A 55-year-old male patient, asymmetric thickening measured as 17.5 mm in the lower thoracic esophagus with a biopsy result of squamous cell carcinoma.

esophagus.[15] The localization of the primary tumor was determined based on the location of the upper margin of the cancer in the esophagus.[15]

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. For the benign-malignant differentiation of the wall thickness, an independent t-test was performed and a receiver operating characteristic (ROC) analysis was made to establish a cut-off value for the ratio of wall thickness and lesion-level thickness to normal segment thickness so as to differentiate between benign and malignant

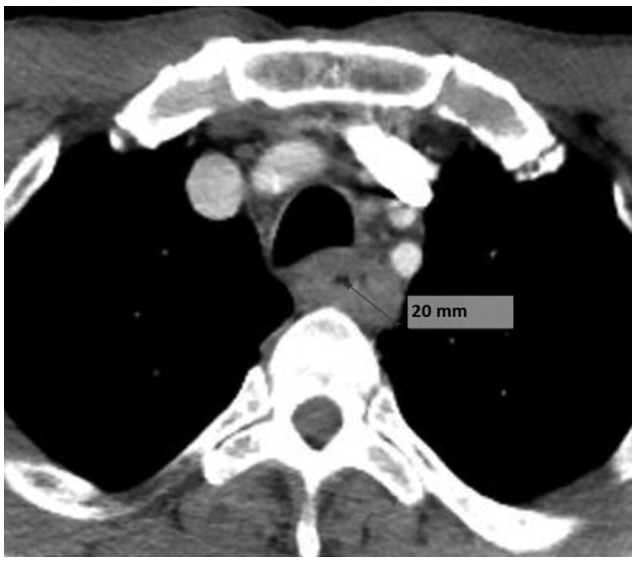

Figure 4. 54-year-old male patient, asymmetric thickening measured as 20 mm in the upper thoracic esophagus with a biopsy result of squamous cell carcinoma.

Figure 5. A 76-year-old male patient, asymmetric thickening measured as 14 mm in the lower thoracic esophagus with a biopsy result of an adenocarcinoma.

Figure 6. A 48-year-old male patient, symmetric thickening measured as 11 mm in the lower thoracic esophagus with an endoscopy result of esophagitis.

Figure 7. A 60-year-old male patient, symmetric thickening measured as 10 mm in the gastroesophageal junction with an endoscopy result of esophagitis.

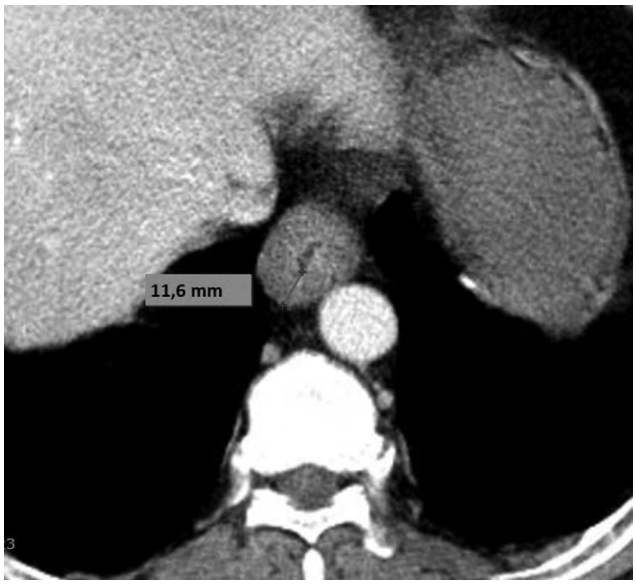

Figure 8. A 53-year-old female patient, symmetric thickening measured as 11.6 mm in the lower thoracic esophagus with a biopsy result of esophagitis.

cases. The chi-square test was performed to identify significant difference between the benign and malignant cases. A *p* value of <0.05 was considered statistically significant.

RESULTS

According to the endoscopy and/or biopsy results, 53 patients had a malignant and 91 patients had a benign pathology. Based on the thickness measurements using CT, the mean thickness of the lesions was 13.78±7.21 mm, with a mean wall thickness of 9.2±1.45 mm and 21.5±6.54 mm in the benign and malignant cases, respectively (Table 1). There was a statistically significant difference in the benign-malignant differentiation (p<0.001).

In the ROC analysis, the cut-off value of the lesion wall thickness for benign-malignant differentiation was established. The area under the curve (AUC) was found to be 0.985 (98.5%). When the best-fit cut-off value was calculated as 13.5 for the AUC, while the sensitivity and specificity were 94.3% and 100%, respectively (Figure 9).

For the benign and malignant cases, the lesion level and the normally observed segment thicknesses were proportioned, with the lesion thickness/normal thickness ratio recorded as 3.57±1.4 in benign cases and 9.25±5.6 in malignant cases (p<0.001).

Asymmetric thickening of the lesion was observed in 94.3% (n=50) of the malignant cases and 5.5% (n=5) of the benign cases. The consistency between malignant thickness increase and asymmetry was found to be statistically significant (p<0.001).

Regarding the distribution of malignant lesions based on anatomical localization, one (1.85%) was in the cervical esophagus, one (1.85%) in the upper thoracic esophagus, 18 (34%) in the medial thoracic esophagus, 18 (34%) in the lower thoracic esophagus, and 15 (28.3%) at the GEJ. Regarding the distribution of benign lesions based on anatomical localization, one (1.2%) was in the cervical esophagus, one (1.2%) in the upper thoracic esophagus, four (4.4%) in the medial thoracic esophagus, and the remaining 85 (94.2%) in the lower thoracic esophagus and/or GEJ.

According to the endoscopy and/or biopsy, the results of the cases in the benign group were as follows: hiatal hernia (n=9), varicose veins (n=8), tertiary contractions (n=5), esophagitis (n=67; 34 not classified, 12 Grade A esophagitis, 13 Grade B esophagitis, 3 Grade C esophagitis, and 5 Candida esophagitis). Two patients were histopathologically diagnosed with Barrett's esophagus.

DISCUSSION

Survival has been shown to prolong in early-diagnosed cases in countries where the disease is endemic[16] and, thus, early diagnosis is crucial. Wall thickening is one of the most significant findings indicating gastrointestinal disease on radiological imaging.[17] The MDCT, in particular, is a highly effective imaging method for the assessment of esophageal wall thickness and edges. Computed tomography is a commonly used preoperative imaging

Table 1. Wall thickness measured using computed tomography

	n	Mean±SD (mm)	Min-Max (mm)	*p*
Benign	91	9.2±1.45	6-13	
Malign	53	21.5±6.54	9.2-38	<0.001
Total	144	13.78±7.21	6-38	

SD: Standard deviation; Min: Minimum; Max: Maximum.

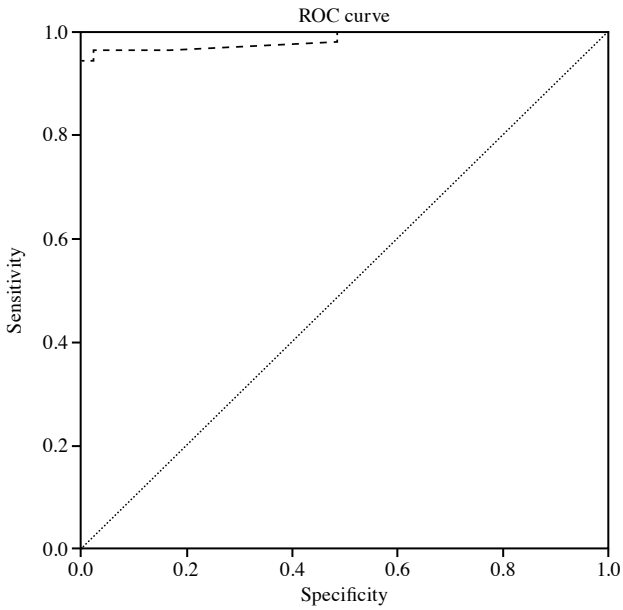

Figure 9. A graph showing ROC curve to discriminate malignancy.
ROC: Receiver operating characteristic.

tool, as the resulting cross-sectional images can show the degree of wall invasion, invasions of adjacent organs, lymph node involvement, and distant metastases in esophageal cancer.[18] In the present study, we also evaluated esophageal wall thickness, as a topic which has seen less scrutiny than the other gastrointestinal tract sections in the literature, using MDCT as a common approach in daily clinical practice. The present study differs in terms of its large case group, and its analysis of all segments of the esophagus. Our study results showed that asymmetric wall thicknesses over 13.5 mm was highly significant in terms of malignancy in tomographic examinations.

In a previous study conducted to determine normal wall thickness through an analysis of esophageal segments on CT among 110 cases with no esophageal disease, nor any complaints suggesting esophageal diseases, the authors concluded that thicknesses exceeding 5.5 mm should be considered abnormal.[19] On the other hand, several researchers suggested that thicknesses exceeding 5 mm should be considered abnormal.[20,21] In the present study, we defined a cut-off wall thickness value of >5 mm.

A very early study reported that asymmetric esophageal thickening might occur in both malignant and benign cases, but provided no specific rates,[13] based on the images of 10-mm section thickness. In the present study, symmetric thickening was noted in 5.7% of the malignant cases, and asymmetric thickening in 94.3%. In the benign cases, asymmetric thickening at the lesion level was observed in 5.5% of cases, and symmetric thickening in 94.5%. This finding indicates a statistically significant consistency between the increase in the esophageal thickness and asymmetry ($p<0.001$).

In another study, the authors investigated the endoscopic correlation of incidental gastrointestinal tract thickness on CT-documented abnormalities from endoscopies of 96% of the patients with sigmoid or rectal thickening, 81% of patients with distal esophageal thickening, and 13% of patients with cecal thickening.[22] The most common pathologies were reported to be esophagitis and rectosigmoid colitis. Malignancy was detected in the cecum in 6% of cases and in the rectosigmoid colon in 13%, while none were detected in the distal esophagus. Also, a pathology was identified in most of the cases in which there was a thickening of the distal esophagus or the rectosigmoid colon, and the authors concluded that the endoscopy was normal in most of the cases with cecal thickening.[22] Based on this finding, any esophageal thickening should be subjected to careful examination.

In the present study, the results of the statistical analysis to establish a cut-off value for lesion wall thicknesses for benign-malignant differentiation using CT were found to be highly significant ($p<0.001$). When the cut-off value was taken as 13.5 mm, sensitivity and specificity were found to be 94.3% and 100%, respectively ($p<0.001$). The difference

Table 2. Demographic features

	Benign patients			Malign patients			Total		
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD
Female	45	49.5		38	71.7		83	58.3	
Male	46	50.5		15	28.3		61	41.7	
The average age (year)			56.0±13.2			59.1±10.6			57.2±12.4

SD: Standard deviation.

in the lesion level-normal segment thickness ratio in benign and malignant cases were also found to be statistically significant ($p<0.001$). This finding supports the significance of CT in patients diagnosed with esophageal cancer.

Esophageal cancer in more common in men than in women and, most frequently, occurs in those over the age of 50 years.[23] In the present study, the female/male ratio was (2.5/1), being more common in women (Table 2), which can be attributed to the local foods consumed at home.

Squamous cell carcinoma is the most common type of esophageal cancer.[23] In the present study, the histopathological examination of esophageal cancers revealed SCC in 79.2%, adenocarcinoma in 13.3%, neuroendocrine tumor in 5.6%, and metastasis in 1.9% of cases. This predominance of SCC is consistent with the literature. As in previous studies, all adenocarcinoma cases were located in the distal (n=7): one in lower esophagus and six in GEJ.

The main limitation of our study is the lack of biopsy results of all patients, as the initial endoscopy did not indicate a requisite. That said, the absence of biopsy results of all patients had no effect on the findings. Another limitation may be the fact that the CT images were not taken based on a specific protocol in terms of the time of contrast agent use.

In conclusion, increases in the esophageal wall thickness and asymmetry detected on computed tomography can contribute to early diagnosis of esophageal cancers, particularly in regions endemic to esophageal cancer, such as our region. We believe that asymmetric wall thicknesses over 13.5 mm may be highly significant in terms of malignancy in tomographic examinations.

Declaration of conflicting interests

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