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Evaluation of Segmental Distribution of Liver Metastases In Colorectal Carcinomas By Computed Tomography

Kolorektal Karsinomlarda Karaciğer Metastazlarının Segmental Dağılımının Bilgisayarlı Tomografi ile Değerlendirilmesi

ABSTRACT Objective:

We aimed to investigate the relationship between the localization of colorectal carcinomas and the topographic distribution of metastatic liver lesions.

Material and Methods:

Patients diagnosed with colorectal cancer and metastatic liver lesions constituted the target population of this study. Demographic data, primary tumor localization, and data regarding liver metastases were retrieved and retrospectively reviewed. Patients' files, endoscopy, and computed tomography reports were analyzed. In addition, data concerning segmental localization of the metastatic liver lesions based on the Couinaud classification were collected.

Results:

Ninety-six patients were diagnosed with colorectal cancer with liver metastases during the study period. A total of 251 metastases were detected. The number of metastases was 169 (67.3%) in the right and 80 (31.9%) in the left lobe (p<0.0001). Evaluation regarding Couinaud classification elucidated that the most frequently affected segment was segment VIII (23.1%), while segment 1 (i.e., caudate lobe) was the least commonly affected segment. The liver segments with the highest number of metastatic lesions were VIII, V, VII, VI, III, II, IV, and I, from greatest to least. There was no significant difference in the segmental distribution of metastases in patients with primary tumors in the right and left colon (p>0.05).

Conclusion:

Liver metastases of colorectal cancer are significantly more common in the right lobe than the left lobe, irrespective of the location of the colorectal tumor. Segment VIII of the right lobe is the main target of metastases.

Key Words:

Colorectal Carcinoma, Liver Metastasis, Segmental Distribution, Couinaud Classification

ÖZ Giriş:

Bu çalışmada kolorektal karsinomlar ile metastatik karaciğer lezyonlarının topografik dağılımı arasındaki ilişki araştırılmıştır.

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Gereç ve Yöntemler:

Kolorektal kanseri ve metastatik karaciğer lezyonları olan hastalar bu çalışmanın hedef popülasyonunu oluşturdu. Demografik veriler, primer tümör lokalizasyonu, ve metastatik karaciğer lezyonlarının segmental dağılımına ilişkin veriler retrospektif olarak tarandı. Hasta dosyaları, endoskopi ve bilgisayarlı tomografi raporları gözden geçirildi. Ek olarak hastaların Couinaud klasifikasyonuna göre belirlenmiş olan metastatik karaciğer lezyonlarının segmental dağılım bilgileri tarandı.

Bulgular:

Doksan altı hastanın karaciğer metastazı yapmış kolorektal kanseri tanısı almış olduğu öğrenildi. Toplamda 251 metastatik karaciğer lezyonu saptandı. Bunların 169 (%67,3) tanesi sağ lobda, 80 (%31.9) tanesi ise sol lobda yer almaktaydı (p<0.0001). Couinaud klasifikasyonuna göre yapılmış olan değerlendirmede en sık etkilenmiş olanın segment VIII (%23.1), en nadir etkilenmiş olanın ise segment 1 (kaudat lob) olduğu anlaşıldı. En sık tutulan karaciğer segmentleri sırasıyla segment VIII, V, VII, VI, III, II, IV, ve segment I'di. Primer tümörü sağ ve sol kolonda olan hastalar kıyaslandığında metastatik lezyonların segmental dağılımı açısından belirgin fark saptanmadı (p>0.05).

Sonuç:

Kolorektal kanserlerin karaciğer metastazları kolorektal tümörün lokalizasyonundan bağımsız olarak daha sağ lobda sol lobdan daha sıktır. Segment 8 en sık tutulan segmenttir.

Anahtar Sözcükler:

Kolorektal Karsinom, Karaciğer Metastazı, Segmental Dağılım, Couinaud Klasifikasyonu

INTRODUCTION

Colorectal carcinoma (CRC) is one of the most common types of cancer and causes of cancer-related death (1). In addition, the liver is the most common site for its metastasis (2,3).

The portal venous system constitutes one of the main routes for liver metastasis of colorectal cancer. Since the portal vein has a specific trajectory in the liver, it can be stated that colorectal cancer cells are conveyed to specific liver segments (4). Although numerous studies aimed to determine the relationship between primary colorectal tumor localization and the topographic distribution of liver metastases, this is still controversial. (5,6). However, it is known that early diagnosis of metastatic disease prolongs patient survival in patients with colorectal carcinoma (7).

Radiological determination of the exact localization of the metastatic liver lesion is also essential for planning the surgical management of these patients (8,9). Based on this assessment, decisions regarding partial hepatectomy, metastasectomy, or interventional radiological methods are also given. It was reported that the 5-year patient survival rate could be increased from 5-10% to 30-40% in patients by liver resection in patients with metastatic colorectal cancer (10).

The Couinaud classification is widely used to describe function-

al liver anatomy (1,11). However, despite the above facts, literature analyzing the distribution of metastatic liver lesions in patients with colorectal cancer based on the Couinaud classification is scarce (3). Therefore, this study aimed to investigate the relationship between the segmental distribution of liver metastases and the primary tumor localization in patients with colorectal cancer.

MATERIALS and METHODS

This research was approved by our institutional ethical review committee (Turkiye Yuksek Ihtisas Hospital Ethical Review Committee- 2019/36). All procedures in this study fulfilled the ethical standards reported in the Helsinki Declaration. Written informed consent was obtained from all study participants. Patients diagnosed with colorectal cancer with liver metastasis constituted the target population of this study. Patient data were retrospectively collected from electronic patient folders. These data included age, gender, primary tumor localization, and the data regarding the segmental distribution of liver metastases. In addition, the endoscopic and radiological data were retrieved from the patients' rectosigmoidoscopy, colonoscopy, and abdominopelvic computerized tomography (CT) reports and images. All abdominopelvic CT scans were performed by the same CT machine (Toshiba Activion 16, TSX-031A, 16-slice multidetector CT). Both unenhanced and enhanced images were obtained, and an experienced hepatobiliary radiologist reviewed all images. Data including localization of the primary colorectal tumor and number, size, and segmental localization of the metastatic liver lesions based on the Couinaud classification, were retrieved by retrospective review of the endoscopy reports and CT images.

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS V21.0, Armonk, NY, US) software. A frequency distribution table was used to analyze the number of occurrences (frequency). In addition, the chi-square test was used to examine the differences between categorical variables to analyze the fit between expected and observed results.

RESULTS

Our retrospective review revealed that 185 patients were diagnosed with colorectal carcinoma during the study period. Among these patients, 96 had liver metastasis. While 63 (65.6%) of these patients were male, 33 (34.4%) were female. The mean age of the male and female patients was 55±6 and 57±7 years. The primary tumor localization of all patients is displayed in Table I.

Table I: Colorectal tumor localizations

Localization	Right-sided colon cancer	Localization	Left-sided colon cancer
	(n=19)		(n=77)
Caecum	5	Descending	17
		colon	
Ascending colon	10	Sigmoid colon	31
Transverse colon	4	Rectum	29

The review of the CT images elucidated that these 96 patients had 251 metastatic liver lesions in total. Among these metastases, 2 (0.8%) were localized in the caudate lobe, 80 (31.9%) in the left lobe, and 169 (67.3%) in the right lobe. The distribution of liver metastases as per primary (i.e., colorectal) tumor localization is exhibited in Table II.

Table II: Distribution of liver metastases as per primary tumor localization

Primary tumor	Segment	Total		
localization	Caudate lobe	Left lobe	Right lobe	
Left colon	1	58	127	186
Right colon	1	22	42	65
Total	2	80	169	251

Fifty-six (70%) of the 80 metastases in the left lobe were in the median segment (i.e., segment IV). Among the 169 metastases in the right lobe, 100 (59.2%) were localized in the anterior segments (segments V and VIII), while 69 (40.8%) were in the posterior segments (segments VI and VII).

Comparison of the right and left lobes regarding the distribution of the metastatic liver lesions revealed that colorectal carcinomas more frequently metastasized to the right lobe (p<0.05). However, there was no difference between the right and left colon tumors in this regard. In 77 patients whose primary tumor was in the left colon, 69% of the liver metastases were located in the right lobe, and 31% were in the left lobe.

No significant difference was found in the segmental distribution of metastases in patients with primary tumors in the right and left colon (p>0.05). However, most metastases were found in the right lobe segments of the liver in both right (127/186; 68%) and left (42/65; 64%) colon tumors.

Evaluation regarding Couinaud classification revealed that the most frequently affected segment was segment VIII (23.1%), while segment 1 (i.e., caudate lobe) was the least commonly affected segment by the distant metastases of colorectal cancer. The rates of metastases to different liver segments are displayed in Table III. In addition, tomographic views of metastatic liver lesions in segments 3 and 7 are shown in Figures 1 and 2.

Table III: Segmental distribution of liver metastases as per Couinaud classification

Parameter	Caudate lobe	Left lobe		Right lobe				
Segment	I	II	III	IV	V	VI	VII	VIII
Number of metastases	2	25	31	24	42	33	36	58
Rate (%)	0.8	10	12.4	9.6	16.7	13.1	14.3	23.1

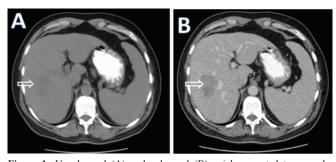


Figure 1: Unenhanced (A) and enhanced (B) axial computed tomography images of a metastatic liver lesion (arrow) in segment 7 of the right lobe

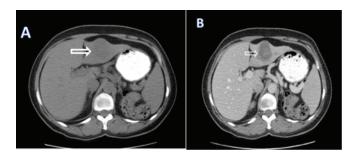


Figure 2: Unenhanced (A) and enhanced (B) axial computed tomography images of a metastatic liver lesion (arrow) in segment 3 of the left lobe

DISCUSSION

The liver is the most common target for metastatic colorectal cancer, and liver metastases play an essential role in the morbidity and mortality of colorectal cancer (12). It was reported that approximately 10% of patients with primary operable colorectal carcinoma already had associated liver metastases at the time of diagnosis. It is also known that the presence of liver metastases significantly worsens the prognosis and decreases the 5-year life expectancy in these patients (13). However, surgical resection is curative in 25% of the patients with isolated hepatic metastasis (14). Furthermore, it was stated that partial hepatic resection increased the 5-year survival rate from 5-10% to 30-40% in colorectal cancer patients with isolated liver metastases (10). In line with the advances in surgical oncology, radiological imaging methods' importance increased in the diagnostic and therapeutic management of these patients (15). Radiological data regarding the number, size, and segmental distribution of metastatic liver lesions can guide the surgical management of these patients. The segmental anatomy of the liver was defined by Claude Couinaud, and the Couinaud classification is widely used for describing the segmental distribution of metastatic liver lesions (16,17). According to this classification, the liver is divided into eight segments by an imaginary line drawn through the hepatic and portal veins (18). This anatomical classification is significantly important because the frequent occurrence of liver metastases in colorectal carcinoma is associated with the anatomy of the blood flow to the liver (19). Of note, most of these metastases occur via the portal venous system.

It is known that the volume and weight of the right lobe of the liver are higher than the left lobe and the right lobe receives more portal blood flow than the left lobe (3). This fact can be considered the reason for detecting metastatic lesions more frequently in the right lobe than the left lobe (2,3,20). Rhu et al. worked on patients with colorectal cancer who had histopathologically confirmed liver metastases (20). Among 652 metastatic lesions, 398 (61%) were in the right liver lobe, while 254 (39%) were detected in the left lobe. They reported that the right-to-left lobe metastatic lesion ratio was 1.57/1. We calculated this ratio as 2.11 (169/80). Similarly, Kadiyoran et al., who evaluated the segmental distribution of liver metastases in colorectal cancer patients, reported that the right-to-left lobe metastatic lesion ratio was 2.35 (21). They also noted that segment VIII was the most frequently involved liver segment in their cohort.

In line with these findings, Holbrook et al., who retrospectively reviewed the patterns of colorectal liver metastases as per Couninaud's segments in 270 patients, documented an overall predominance of the right liver lobe metastases irrespective of the site of the primary colorectal cancer (22). These authors reported that segment VIII was the most frequently involved liver segment in their cohort. The involvement rate of this right lobe segment was calculated as 15,3%. In our study, segment 8 was also the most commonly affected liver segment, with an involvement rate of 23,1%. The rate of metastasis to the right liver lobe was significantly higher than the left lobe in our study. This result is consistent with several previously published reports (2,3,20,21).

In the literature, there are several reports regarding the distribution of liver metastasis and the relation of these metastases to portal circulation (23-25). Some of these studies referred to double circulation theory and suggested that the distribution of liver metastases was characterized by a specific pattern. For example, Moore and Bridenbaugh et al., who investigated the distribution of portal blood flow in the liver using portal venography, showed that a significant portion of the splenic venous inflow was distributed to the left lobe of the liver (25). In contrast, most of the blood from the superior mesenteric vein was distributed to the right lobe of the liver.

Serege et al., who defined the streamline phenomenon, reported that colorectal tumor cells reached specific liver regions depending on whether the portal venous drainage of the primary tumor was via the superior mesenteric or the inferior mesenteric vein (24). These authors reported that the bloodstream from the superior mesenteric vein (SMV) supposedly flowed more along the right margin of the portal vein (PV) to the right lobe of the liver. In contrast, blood from the inferior mesenteric vein (IMV) flowed more along the left margin of the PV, draining into the left lobe of the liver. The streamline phenomenon is based on the fact that the SMV is a straight upward continuation of the PV, while the IMV hinged at a 90° angle to join the splenic vein (SV) (4,24). This phenomenon was related to the distribution of the liver metastases of the mesenteric tumors (26).

Shirai et al. tested the streamline phenomenon with a study including 85 patients with liver metastasis originating from colorectal cancer and underwent curative hepatectomy (27). While 18 patients had a right colon tumor, 67 had a left-sided colon tumor. One hundred and 95 metastatic deposits were detected in these patients; 135 were in the right lobe, and 60 were in the left lobe. In the right colon tumor group, 29 metastatic lesions were in the right liver lobe, while three were in the left. On the other hand, in the left colon tumor group, 106 metastatic foci were in the right lobe, and 57 were in the left lobe. Comparison of the metastatic lesions' distribution between patient groups with right and left colonic tumors revealed a significant difference regarding lobar distribution. They concluded that right colon cancers selectively involved the right lobe, while left colonic tumors involved the entire liver. Their findings supported the streamline phenomenon (24).

While it can be stated that the streamline phenomenon did not have clinical significance, it is known that it has great significance in portal circulation (20,24). The concept of streamlining suggests that the venous flows from the SMV and IMV are not fully mixed in the PV, resulting in a disproportionate blood flow to the right and left lobes of the liver. The streamline phenomenon explains the fact that right colon tumor cells can reach the right lobe of the liver through the SMV, and therefore the risk of metastasis to the right liver lobe is increased in these patients. However, this phenomenon cannot explain why left colon tumors predominantly metastasize to the right liver lobe. The fact that IMV usually joins the portal venous system at the level of or near the splenomesenteric junction and the exact location where the IMV opens to the portal venous system varies between patients should be considered while making decisions based on this phenomenon (24,28).

Aktan et al. conducted an autopsy study including 60 cases and reported that IMV opened to the SV in 56.3%, the SMV in 31.3%, and the splenomesenteric junction in 12.5% of the subjects (29). When these results are considered along with the streamline phenomenon, it can be proposed that more than 60% of the left colon tumors will metastasize to the left lobe of the liver via the IMV, which opens to the SV at a rate of 56.3% and the splenomesenteric junction at a rate of 12.5%. However, our study showed that left colon tumors metastasized to the right liver lobe in 69% and the left liver lobe in 31% of the patients. These findings do not align with the results Aktan et al. reported (29)

Some studies investigating the liver metastases of colorectal tumors focused on the weight and volumes of the liver lobes (3,6). In one of these studies, Schulz et al. detected that the ratio of the weight and volume of the right lobe of the liver to the weight and volume of the left lobe was 2:1 (6). Based on this finding, it was hypothesized that liver metastases occurring via the PV showed a homogeneous distribution, and thus the rate of right liver lobe metastases was twice as high as that of the metastases in the left lobe. Our results support this hypothesis since the ratio of the number of metastases observed in the right liver lobe to those in the left liver lobe was 2,11/1 in our cohort. Moreover, this ratio was similar in right and left colon tumors, with the former being 1.96/1 and the latter 2.18/1. These results are comparable to those obtained in the autopsy studies (29).

Desai et al. investigated the distribution of colorectal tumor metastases in the liver and found a significant relationship between the localization of the colorectal tumor and the distribution of liver metastases (4). Our study showed no significant difference regarding the segmental distribution of metastases in patients with primary tumors in the right and left colon. However, it showed that the direction of portal blood flow might be associated with the distribution of liver metastases and that the right colon tumors mostly metastasized to the right liver lobe. Similarly, liver metastases of the left colon carcinomas were mainly in the right liver lobe. Since the volume of the right liver lobe is twice as much as the left liver lobe and the diameter of the right PV is significantly larger than the left PV, and the exact location of the opening of IMV to the portal venous system varies from person to person; it can be concluded that left colon tumors may also metastasize to the right liver lobe.

Although numerous studies investigated the relationship between colorectal tumor localization and the topographic distribution of liver metastases, they did not reach a common conclusion (4,21,22,27). However, determining the distribution of liver metastases is very important in patients with colorectal cancer since the success of surgical resection depends on the number and localization of the metastatic lesions (30). Our study revealed that liver metastases were localized 2,1 times more frequently in the right liver lobe than the left liver lobe and that the main target was segment VIII of the right lobe, irrespective of the location of the primary colorectal tumor.

Our study has some limitations that must be considered while evaluating its findings. First, it is a retrospective study that could be affected by all inherent weaknesses stemming from its retrospective design. Second, the metastatic lesions were only radiologically confirmed, and a histopathological confirmation process was not included in the analysis. Third, radiological interpretations were performed by one expert hepatobiliary radiologist; the risk of interobserver variability could have been acknowledged if two radiologists had done the assessments.

CONCLUSION

Despite the weaknesses mentioned above, we conclude that liver metastases are more frequently encountered in the right lobe than the left lobe and segment VIII is the most common site for metastatic lesions. Therefore, in cases with indeterminate liver lesions detected on CT scans of patients with colorectal cancer, there should be high suspicion of metastasis if the lesion is in the right lobe, particularly in segment VIII. The location of the primary colorectal tumor should not affect this approach.

Ethical Committee Approval

This research was approved by our institutional ethical review committee (Turkiye Yuksek Ihtisas Hospital Ethical Review Committee- 2019/36). All procedures in this study fulfilled the ethical standards reported in the Helsinki Declaration.

Informed Consent:

Written informed consent was obtained from all study participants according to the Helsinki Declaration.

Author Contributions:

Concept: N.K.S., G.K. Design: N.K.S., K.N.A. Supervision: N.K.S., G.K. Resources: N.K.S., K.N.A. Materials: G.K., K.N.A. Data Collection and Processing: G.K., K.N.A. Analysis or Interpretation: N.K.S., K.N.A. Literature Search: G.K., K.N.A. Writing Manuscript: N.K.S., G.K. Critical Review: N.K.S., G.K.

Conflicts of Interest:

The authors declare no conflicts of interest

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