

## T3 TRANSVERSE COLON TUMORS: DIFFERENCES OF THE SAME COLON SEGMENTS WITH TWO DIFFERENT EMBRYOLOGICAL ORIGINS

T3 TRANSVERS KOLON TÜMÖRLERİ: İKİ FARKLI EMBRİYOLOJİK ORİJİNİNDEN GELİŞEN AYNI KOLON SEGMENTİ TUMORLERİN FARKLARI

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**Keywords:** Colorectal cancers, transvers colon, embryological, midgut, hindgut

**Anahtar Sözcükler:** Kolorektal kanserler, transvers kolon, embriyolojik, midgut, hindgut

Yazının alınma tarihi: 31.01.2022

Yazının kabul tarihi: 01.06.2022

Online basım: 31.07.2022

### SUMMARY

**Introduction:** Transverse colon tumors constitute approximately 10% of colon tumors. The aim of this study is to investigate the clinicopathological features of tumors located in the distal 1/3 and proximal 2/3 of the transverse colon in terms of embryological development in T3 colon cancers.

**Material and Method:** 52 patients with pathological stage pT3 were included in the study. The patients were divided and evaluated in 2 groups according to the tumor localization in the transverse colon, as proximal 2/3 (group-1) and distal 1/3 (group-2). The patients were compared in terms of tumor volume, lymph node involvement, number of removed lymph nodes, the histological grade of the tumor, liver metastasis and survival.

**Results:** The mean tumor volume was found statistically significantly higher in group 1 than in group 2 ( $p: 0.001$ ). The number of removed lymph nodes was higher in group-1 than group-2, and this result was found statistically significant ( $p: 0.002$ ). There was no significant difference in overall survival between the groups ( $p: 0.35$ ). Lymph node positivity has been detected to decrease 5-year survival rates ( $p: 0.03$ ).

**Conclusion:** Although the tumors located to transverse colon have similar clinicopathological features to the colon segment in which they are included, the proximal does not act like right colon tumors and distal does not act like left colon tumors. The question of "Can transverse colon tumors be evaluated separately as right and left colon tumors?" will find the answer with larger studies.

### ÖZ

**Giriş:** Transvers kolon tümörleri, kolon tümörlerinin yaklaşık %10'unu oluşturur. Bu çalışmanın amacı T3 transvers kolon kanserlerinde kolonun distal 1/3 ve proksimal 2/3'ünde yer alan tümörlerin embriyolojik gelişim açısından klinikopatolojik özelliklerini araştırmaktır.

**Gereç ve Yöntem:** Patolojik evre pT3 olan 52 hasta çalışmaya dahil edildi. Hastalar transvers kolondaki tümör yerleşimine göre proksimal 2/3 (grup-1) ve distal 1/3 (grup-2) olmak üzere 2 gruba ayrılarak değerlendirildi. Hastalar tümör hacmi, lenf nodu tutulumu, çıkarılan lenf nodu sayısı, tümörün histolojik derecesi, karaciğer metastazı ve sağ kalım açısından karşılaştırıldı.

**Bulgular:** Ortalama tümör hacmi grup 1'de grup 2'ye göre istatistiksel olarak anlamlı derecede yüksek bulundu ( $p: 0,001$ ). Çıkarılan lenf nodu sayısı grup-1'de grup-2'ye göre daha fazlaydı ve bu sonuç istatistiksel olarak anlamlı

bulundu ( $p: 0,002$ ). Gruplar arasında genel sağkalım açısından anlamlı fark yoktu ( $p: 0,35$ ). Lenf nodu pozitifliğinin 5 yıllık sağ kalım oranlarını azalttığı tespit edilmiştir ( $p: 0,03$ ).

**Sonuç:** Transvers kolona yerleşimli tümörler dahil oldukları kolon segmenti ile benzer klinikopatolojik özelliklere sahip olmalarına rağmen proksimal sağ kolon tümörleri gibi, distal ise sol kolon tümörleri gibi hareket etmez. "Transvers kolon tümörleri sağ ve sol kolon tümörleri olarak ayrı ayrı değerlendirilebilir mi?" sorusunun cevabı daha büyük çalışmalarla bulunabilecektir.

## INTRODUCTION

In terms of frequency, colorectal cancers are in 3rd place in men and 2nd place in women worldwide. Recent publications show differences between right and left colon cancers in terms of epidemiology, clinic, pathology and genetic (1,2). Right colon cancers have different molecular development steps and are more common in women and at older ages. Also, the right colon cancers have larger sizes and diagnosed in advanced stages (3). The prognostic effects of tumor location in colon cancer have been inclusively investigated (4). Most studies have shown worse survival rates in right colon cancer than left colon cancer (5,6). During embryological development, it is known that the proximal two-thirds of the transverse colon originates from the midgut, and distal one-third originates from hindgut (7). Some differences between the right and left colon are known, but the differences between the proximal and distal transverse colon can be explored like the right and left colon. As far as we know, there is no study investigating the clinicopathological features of transverse colon tumors. The aim of this study is to investigate the clinicopathological features of tumors located in the distal 1/3 and proximal 2/3 of the transverse colon in terms of embryological development in T3 colon cancers.

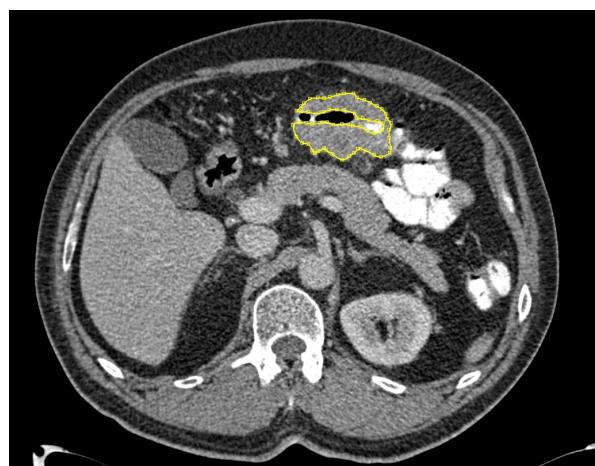
## MATERIAL AND METHOD

The cases operated on with the diagnosis of colon cancer between January 2012 and January 2020 were evaluated retrospectively. The research was conducted according to the World Health Organization Helsinki Declaration "Ethical Principles for Medical Research Involving Human Subjects". The approval of the local ethics committee was obtained for the study. 52 patients with pathological stage pT3 adenocarcinomas, older than 18 years old, who has transverse colon (between hepatic flexure-splenic flexure) malignities were included in the study. Patients with synchronous tumors or another solid organ

tumor, recurrence tumoral lesions, younger than 18 years old, who has polyposis syndromes were excluded from the study. The patients were divided and evaluated in 2 groups according to the tumor localization in the transverse colon, as proximal 2/3 (group-1) and distal 1/3 (group-2). The patients were compared in terms of age, gender, tumor volume, lymph node involvement, number of removed lymph nodes, the histological grade of the tumor, liver metastasis, follow-up period, survival, and operation method.

## Radiological Interpretation

Abdominal computerized tomographies of all patients were evaluated by a single radiologist and volume calculation was performed. Tumor volume was assessed on post-contrast CT images. For volume calculation, tumor boundaries were drawn in the workstation using an interactive manual software program. The tumor volume was automatically calculated by the software program by multiplying the cross-sectional area by section thickness (Figure 1).



**Figure 1.** Tumor volume measurement with computed tomography.

## Statistical analysis

Social Sciences Statistics Package (SPSS 21 Inc., Chicago, IL, USA) computer software was used

for bio-statistical analysis. Categorical variables were presented as frequency (percentage), and continuous variables were reported as mean  $\pm$  standard deviation. Differences in patients' characteristics between Group-1 and Group-2 were examined by Pearson's chi-square test for categorical variables, and by Mann Whitney test and for numerical variables. Kaplan-Meier curves for overall-free survival were compared by the log-rank test.

## RESULTS

The sociodemographic features of the patients are summarized in Table 1. From 1315 patients who were operated with the diagnosis of colon cancer, 52 patients (34 males, 18 females) with pT3 tumor localized in the transverse colon were included in the study. The average age of patients was  $66.7 \pm 12$  (38-84). The mean tumor volume was determined as  $51949 \text{ mm}^3$  (8551-250005 mm $^3$ ). The mean number of removed lymph nodes was  $19 \pm 9.3$  and the mean number of positive lymph nodes was  $1.5 \pm 2.7$ . The mean follow-up period was  $12 \pm 10.3$  months. The metastatic lymph node was detected in 42.3% of the patients. Liver metastasis was detected in 10 patients (19.2%). In 34 (65.4%) of the cases, the tumor was localized in the proximal 2/3 of the transverse colon and 18 (34.6%) localized in the distal 1/3 (Table 1). The mean tumor volume was found statistically significantly higher in group 1 than in group 2 ( $p: 0.001$ ). There was no significant difference between the groups in terms of lymph node positivity ( $p: 0.23$ ). The number of removed lymph nodes was higher in group-1 than group-2, and this result was found statistically significant ( $p: 0.002$ ). The emergency surgical operations rate in group 2 was significantly higher because of obstruction when compared to group 1 ( $p: 0.001$ ) (Table 2).

The mean follow-up period was 24 (1-37) months, and the mean survival was  $28.6 \pm 2.9$  months. There was no significant difference in overall survival between the groups ( $p: 0.35$ ). The mean survival was  $15.6 \pm 4.2$  months in patients with positive lymph nodes and  $33.7 \pm 3.9$  months in patients with a negative lymph node. Lymph node positivity has been detected to decrease 5-year survival rates ( $p: 0.03$ ).

**Table 1.** Demographics and pathological characteristics

Sex	n%
Female	18 (34.6%)
Male	34 (65.4%)
Tumor location	
2/3 of the transverse colon proximal-right colon	34 (65.4%)
1/3 of the transverse colon distal-left colon	18 (34.6%)
TNM stage	
Stage 2	26 (50%)
Stage 3	18 (34.6%)
Stage 4	8 (15.4%)
Grade	
Well differentiated	22 (42.3%)
Moderately differentiated	26 (50%)
Poorly differentiated	4 (7.7%)
T stage	
T3	56 (100%)
N stage	
N0	30 (57.7%)
N1	14 (26.9%)
N2	8 (15.4%)
M stage	
M0	44 (84.6%)
M1	8 (15.4%)

TNM = tumor, nodal status, metastasis.

**Table 2.** Characteristics and comparison between patients with 2/3 of the transverse colon proximal and 1/3 of the transverse colon distal.

Variables	2/3 of the transverse colon proximal, % (n = 34)	1/3 of the transverse colon distal, % (n = 18)	p-value
Age:			
- Median (mean) age	64.7	71.7	0.008
Gender:			
- Male	70.6 (24)	55.6 (10)	0.28
- Female	29.4 (10)	44.4 (8)	
Surgical emergency:			
- Yes	17.6 (6)	66.7 (12)	0.001
- No	82.4 (28)	33.3 (6)	
<12 lymph nodes examined:			
- Yes	0 (0)	33.3 (6)	0.001
- No	100 (34)	66.7 (12)	
pN+:			
- N0 (0)	52.9 (18)	66.7 (12)	
- N1 (1–3)	29.4 (10)	22.2 (4)	
- N2 (>3)	17.6 (6)	11.1 (2)	0.001
Stage:			
- Stage II	47.1 (16)	55.6 (10)	
- Stage III	41.2 (14)	22.2 (4)	
- Stage IV	11.8 (4)	22.2 (4)	0.32
Tumor volume:			
- Median volume	72334	17002	0.001

## DISCUSSION

Colorectal cancers are one of the most frequently diagnosed cancers worldwide, and more than 600,000 patients die from this cancer each year. Transverse colon tumors constitute approximately 10% of colon tumors. Right colon tumors have typically bulky, exophytic and polypoid structures that grow towards the lumen. Left colon tumors often infiltrate the lumen and cause obstruction (8,9). In our study, the rate of emergency surgical operations was significantly higher in group 2 because of obstruction when compared to group 1 (p: 0.001).

In a conducted study, more than 300,000 cases of colon cancer were examined and 48% of cases were reported to be located in the right colon (midgut) and 52% in the left colon (hindgut) (10). In another study, approximately 45.1% of colon cancers were localized in the right colon and 54.9% localized in the left colon (4). In our study, unlike the rates of right and left colon tumors in the literature, 65.4% of our cases were located in the proximal 2/3 of the transverse colon (midgut) and 34.6% were located in the distal 1/3 of the transverse colon (hindgut).

Like many other solid tumors, lymph node involvement is one of the strongest prognostic variables in colon cancer and indicates poor prognosis (10,11). Lymph node involvement is more common in right colon tumors and the stage of the disease has been reported to be more advanced than the left colon (7). In our study, there was no difference between the groups in terms of lymph node positivity (p: 0.23). In patients with lymph node involvement, the 5-year survival rate was found to be decreased (p: 0.03).

Many studies have shown that the stage of the disease is associated with the degree of lymphadenectomy. The number of examined lymph nodes has increased with stage, and patients who have operated on stage III and above have a higher number of lymph nodes removed (12). 50% of our cases were at stage II, 34.6% were at stage III, 15.4% were at stage IV. We determined our average lymph node number as  $19 \pm 9.3$ . We think that our lymph node number is high because the majority of our cases are at stage III and IV.

In right colon cancer cases, more lymph nodes are collected than left colon cancer or rectal cancers (13). This observation may be partially related to the longer duration of right-sided surgical resections. It is assumed that tumor necrosis increases due to exposure of the host immune system to tumor antigens (14,15). This mechanism may explain why larger or higher T stage tumors are associated with higher lymph node collection (14). The number of lymph nodes removed in our study was significantly higher in Group 1 ( $p: 0.002$ ). Again, when the tumor volume was compared, it was significantly higher in group-1 ( $p: 0.001$ ).

Another reason for the high number of lymph nodes collected in our study is that the patients included in the study were pT3 (16). In our study, the cases were divided into three groups according to the N stage. A comparison was made in terms of removed lymph nodes number and no significant difference was found between the groups, unlike the literature ( $p: 0.02$ ).

The limitations of our study are; The study includes the small number of patients and the study includes only pT3 tumors to standardize. So that, N stage comparisons for both groups may be different in other stages.

Publications are reporting that tumor placement is age related. Right colon tumors have been reported to be more common in the elderly and women (10). In our study, there was no difference in tumor placement according to gender ( $p: 0.28$ ). In our study, unlike the literature, it was found that tumors originating from the distal 1/3 half of the transverse left colon were seen more common at older ages. ( $P = 0.008$ ).

Five-year survival ranges from 92% in stage I to 11% in stage IV. (13). In our cases, we found 5-year survival as 70% in stage II tumors, 50% in stage III and 25% in stage IV tumors. Meguid and colleagues analyzed 77,987 patients with colorectal cancer and found that the prognosis was worse in the right colon cancers (14). Zenger and colleagues find that on their clinical series right colon stage 3 tumors worse than left colon

tumors (16). Karatas and his friends reported that in their study primary tumor localization was not an important factor on survival in patients with early colorectal cancer (17). In contrast, there are some studies reporting that the prognosis is worse in left colon cancers (3). In our study, there was no difference between the groups in overall survival ( $p: 0.35$ ) (Figure 2).

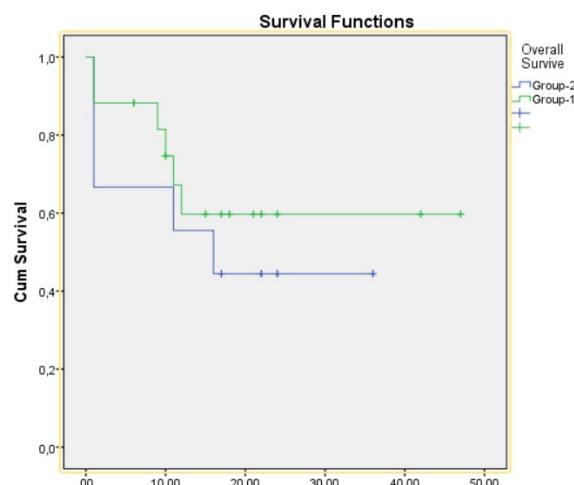


Figure 2. Overall survival comparison between groups.

## CONCLUSION

The distal 1/3 of the transverse colon included to the left colon and the proximal 2/3 included the right colon. Although the tumors located to transverse colon have similar clinicopathological features to the colon segment in which they are included, the proximal does not act like right colon tumors and distal does not act like left colon tumors. Tumors distal and proximal of the transverse colon are mostly seen in elderly patients. There was no difference between distal and proximal cancer patient groups in terms of lymph node positivity and survival. In proximal cancer patients, tumor volume is larger and the number of removed lymph nodes is higher, and obstruction findings are more common in distal cancer patients.

The question of “Can transverse colon tumors be evaluated separately as right and left colon tumors?” will find the answer with larger studies.

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