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Comparison of pathologies in patients operated for transverse colon tumor with embryogenic and anatomical insights

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ABSTRACT

Aims: Transverse colon cancers account for only about 10% of all colon cancers. It is generally known that proximal and distal colon tumours have different genetic and biological features. He transverse colon serves as the division point between proximal and distal regions. In this study, transverse colon cancer was classified both embryologically and anatomically, and a comparative analysis was conducted based on pathological results.

Methods: A retrospective study was conducted on patients who underwent surgery for transverse colon cancer at Ankara Bilkent City Hospital between 2019 and 2023. Patients were classified embryologically as proximal (Group A) and distal (Group B), and anatomically as hepatic angle (Group 1), middle (Group 2), and splenic angle (Group 3), and pathological results were compared among these groups.

Results: For embryogenic classification in terms of the final pathological staging, group A had 1 (1.47%) in Stage 1, 32 (47.05%) in Stage 2, 26 (38.23%) in Stage 3, and 9 (13.23%) in Stage 4. Group B had 2 (2.54%) in Stage 1, 29 (50%) in Stage 2, 20 (34.48%) in Stage 3, and 7 (12.06%) in Stage 4. There was no significant difference between the groups. For anatomical classification , the number of patients in Stages 1, 2, 3, and 4 for groups 1, 2, and 3 were as follows: Stage 1: 2 (3.5%), 1 (3.57%), 0 (0%); Stage 2: 29 (50.87%), 17 (60.81%), 15 (37.5%); Stage 3: 20 (35.7%), 7 (25%), 19 (47.5%); Stage 4: 7 (12.28%), 3 (10.71%), 6 (15%). There was no statistically significant difference between the groups ($p>0.05$).

Conclusion: The pathological results and stages of transverse colon cancers classified embryologically and anatomically showed no significant differences among the groups.

Keywords: Colon cancer, transverse colon, embriology, anatomy

INTRODUCTION

Colorectal carcinoma constitutes approximately 10% of all carcinomas and ranks as the third most commonly diagnosed cancer, with the fourth highest mortality rate.[1] Neoplasms located proximally and distally in the colon exhibit molecular, biological, anatomical and embryological differences.[1,2] Transverse colon cancers, on the other hand, are situated right in the middle between proximal and distal (or right/left) colon tumors and have been reported to have a poorer prognosis compared to cancers in other regions.[3] The complex embryology and anatomy of the transverse colon, which originates from the junction of the midgut and foregut and is in close proximity to foregut-derived organs such as the pancreas, omentum, and stomach, are believed to contribute to the unfavorable prognosis of transverse colon cancers.[3] Furthermore, the classification of the transverse colon as either proximal or distal has been deemed problematic, as evidenced by its exclusion in the CALGB80405 study conducted by Venook.[2]

The surgical management of transverse colon cancers is a subject of debate; however, the generally accepted surgical treatment is Complete Mesocolic Excision (CME). CME is considered the standard treatment for colon cancers.[4] The goal of CME is to ligate at their roots the arteries that feed the relevant part of the colon and eliminate the region with the same embryological base.[5] Resection with embryological integrity and central vascular ligation lowers recurrence not only in the rectum but also in other colon segments.[4-6] Transverse colon tumors are treated with different surgical procedures depending on their localization. Tumors near the hepatic angle are treated with extended right hemicolectomy, those near the splenic angle undergo extended left hemicolectomy, and medial tumors are managed with transverse colectomy. Consequently, different embryogenic tissues and arteries are included in the specimen.[3] These treatments can be carried out through open, laparoscopic, or robotic approaches and have equivalent oncological outcomes.[5,7,8]

Due to the anatomical and embryological characteristics of the transverse colon, as well as its propensity for invasion of adjacent organs and extra-mesenteric lymph node metastasis, managing transverse colon cancer poses additional challenges.[9]

The challenges in the treatment of transverse colon cancers due to their unique characteristics are well-known. However, there have been no reported differences within transverse colon tumors based on their classification and pathological results. In this study, transverse colon tumors were classified embryologically as cancers originating from the midgut and hindgut, and anatomically as tumors located in the hepatic angle, splenic angle, and medial regions. The aim was to compare pathological results within these classifications.

METHODS

A retrospective analysis was conducted on 126 patients who underwent extended right hemicolectomy, extended left hemicolectomy, and transverse colectomy due to hepatic angle, splenic angle, and transverse colon tumors at Ankara Bilkent City Hospital between May 2019 and May 2023. Approval number E1-23-3693 was received for the study from Ankara Bilkent City Hospital Ethics Committee (Date: 19.06.2023). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The patients' demographic characteristics, preoperative stages, pathological findings, morbidity, and mortality data were examined. Patients who underwent these procedures for reasons other than benign causes, hepatic angle, transverse colon, and splenic angle tumors were not included in the study.

The patients were classified anatomically as Group 1 for hepatic angle tumors, Group 2 for transverse colon tumors, and Group 3 for splenic angle tumors. They were also classified embryologically as Group A for tumors originating from the midgut and Group B for tumors originating from the hindgut. The groups that were separated anatomically and embryologically were compared with each other in terms of preoperative hematological parameters, tumor markers, clinical stages, surgical margin positivity, the number of removed lymph nodes, and pathological stages.

Inclusion and Exclusion Criteria

All patients over the age of 18 who were diagnosed with transverse colon cancer and operated on were included. Patients who underwent transverse colon resection for another reason, resection for palliation, or patients who did not undergo oncological resection were not included in the study.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics, including mean age, gender distribution, and more. The chi-squared test was applied to assess whether there was a significant relationship between anatomical groups (Group 1, 2, 3) and gender distribution. An independent samples t-test was utilized to determine if there was a significant age difference between embryological groups (Group A vs. Group B). Analysis of Variance (ANOVA) was conducted to examine if anatomical groups had varying impacts on the number of lymph nodes removed. Additionally, a Mann-Whitney U test was employed to compare tumor stage distribution between embryological groups (Group A vs. Group B). Lastly, a chi-squared test was used to investigate associations between anatomical groups and final pathological stages. The data analysis was conducted using the IBM SPSS Statistics 23 statistical package software (IBM Corp., Armonk, NY, 2016). In the study, the significance level was set at $p<0.05$.

RESULTS

Embryological Classification

Embryologically, there were 68 patients in Group A and 58 patients in Group B, and there was no statistically significant difference between them ($p>0.05$). The mean age of Group A was 67.2, and Group B was 66.4, with no statistical difference between the groups ($p>0.05$). Of the total 126 patients, 44 (34.64%) were female, and 83 (65.36%) were male. Among female patients, 22 (50%) were of midgut origin, while the other 50% were of hindgut origin. Among male patients, 47 (56.62%) were of midgut origin, and 36 (43.38%) were of hindgut origin, and no statistically significant difference was found ($p>0.05$) (Table 1).

Table 1. Demographic data and preoperative stages

	Embryologic Classification		Anatomic Classification		
	A (n:68)	B (n:58)	1 (n:57)	2 (n:29)	3 (n:40)
Age	67.2	66.4	68.1	68	64.9
Gender					
Female	22 (50%)	22 (50%)	22 (50%)	9 (20.45%)	13 (29.55%)
Male	47 (56.62%)	35 (43.38%)	35 (43.38%)	20 (29.85%)	27 (40.29%)
Preoperative stage					
1	10 (14.70%)	8 (13.79%)	8 (13.9%)	4 (14.28%)	6 (15%)
2	35 (51.47%)	29 (50%)	29 (51.25%)	16 (57.14%)	19 (47.50%)
3	16 (23.52%)	16 (27.58%)	16 (27.58%)	5 (17.85%)	1 (2.75%)
4	7 (10.29%)	5 (8.49%)	5 (8.62%)	3 (10.61%)	4 (10%)

Of the tumors originating from the midgut, 10 (14.70%) were in Stage 1, 35 (51.47%) were in Stage 2, 16 (23.52%) were in Stage 3, and 7 (10.29%) were in Stage 4. Among tumors originating from the hindgut, 8 (13.79%) were in Stage 1, 29 (50%) were in Stage 2, 16 (27.58%) were in Stage 3, and 5 (8.49%) were in Stage 4. There was no significant difference detected between the stages of Groups A and B ($p>0.05$).

When evaluating the pathological results, it was found that in Group A, the average number of lymph nodes removed was 19, while in Group B, it was 14.2. In Group A, 20 (29.41%) had Grade 1 differentiation, 31 (45.58%) had Grade 2, 12 (17.64%) had Grade 3, and 5 (7.35%) had Grade 4. In Group B, 17 (29.31%) had Grade 1 differentiation, 29 (50%) had Grade 2, 9 (15.51%) had Grade 3, and 3 (5.17%) had Grade 4. There was no statistically significant difference in any of these data. The circumferential margin was positive in only 1 (1.47%) patient in Group B, with no positive cases in Group A. Both groups had negative proximal and distal surgical margins. Macroperforation was detected in 1 (1.47%) patient in Group A and 1 (1.72%) patient in Group B, with no significant difference between the groups ($p>0.05$). The presence of perineural invasion, perivascular invasion, tumor deposits, and peritoneal invasion in Group A and B

was as follows: 28 (42.17%) and 21 (36.20%), 34 (50%) and 27 (46.55%), 18 (26.47%) and 17 (29.31%), 7 (10.21%) and 2 (3.44%), respectively, and there was no difference between the groups (p>0.05). In terms of the final pathological staging, Group A had 1 (1.47%) in Stage 1, 32 (47.05%) in Stage 2, 26 (38.23%) in Stage 3, and 9 (13.23%) in Stage 4. Group B had 2 (2.54%) in Stage 1, 29 (50%) in Stage 2, 20 (34.48%) in Stage 3, and 7 (12.06%) in Stage 4. There was no significant difference between the groups. (Table 2)

Table 2. Comparison of pathologic results between embryologic class

	Group A	Group B
NHLN	19	14.2
Differentiation		
Grade 1	20 (29.41%)	17 (29.31%)
Grade 2	31 (45.58%)	29 (50%)
Grade 3	12 (17.64%)	9 (15.51%)
Grade 4	5 (7.35%)	3 (5.17%)
Surgical margin tumor		
Proximal	0	0
Distal	0	0
Circumpharantial	0	1 (1.47%)
Perineural invasion	28 (42.17%)	21 (36.20%)
Perivascular invasion	34 (50%)	27 (46.65%)
Tumor deposit	18 (26.47%)	17 (29.31%)
Peritoneal invasion	7 (10.21%)	2 (3.44%)
Patologic stage		
1	1 (1.47%)	2 (2.54%)
2	32 (47.05%)	29 (50%)
3	26 (38.23%)	20 (34.48%)
4	9 (13.23%)	7 (12.06%)

Anatomical Classification

In the anatomical classification, the number of patients in Groups 1, 2, and 3 was 57, 29, and 40, respectively, and there was no statistically significant difference (p>0.05). The mean ages of these groups were 68.1, 68, and 64.9, respectively, and no statistically significant difference was found (p>0.05). In Group 1, there were 22 (50%) female and 35 (43.38%) male patients; in Group 2, there were 9 (20.45%) female and 20 (29.85%) male patients; and in Group 3, there were 13 (29.55%) female and 27 (40.29%) male patients. There was no significant difference in gender among the groups (p>0.05).

In Group 1, 8 (13.79%) patients were in Stage 1, 29 (51.25%) were in Stage 2, 16 (27.58%) were in Stage 3, and 5 (8.62%) were in Stage 4. In Group 2, 4 (14.28%) patients were in Stage 1, 16 (57.14%) were in Stage 2, 5 (17.85%) were in Stage 3, and 3 (10.71%) were in Stage 4. In Group 3, 6 (15%) patients were in Stage 1, 19 (47.5%) were in Stage 2, 1 (2.75%) was in Stage 3, and 4 (10%) were in Stage 4. When the stages of Groups 1, 2, and 3 were compared, no significant difference was found between them (p>0.05). (Table 3)

When comparing pathological results, it was found that Group 1 had an average of 19.6 lymph nodes removed, Group 2 had an average of 16.1, and Group 3 had an average of 13.6 lymph nodes removed. There was no statistically significant difference between the groups (p>0.05). In terms of grade differentiation, Group 1 had 17 (29.82%) with Grade 1 differentiation, 29 (51.25%) with Grade 2, 9 (15.78%) with Grade 3, and 3 (5.26%) with Grade 4. Group 2 had 11 (39.28%) with Grade 1 differentiation, 11 (39.28%) with Grade 2, 5 (17.85%) with Grade 3, and 1 (3.57%) with Grade 4. Group 3 had 9 (22.5%) with Grade 1 differentiation, 20 (50%) with Grade 2, 7 (17.5%) with Grade 3, and 4 (10%) with Grade 4. There was no significant difference between the groups in terms of grade differentiation (p>0.05). Only one patient in Group 3 (2.5%) had a positive circumferential margin. In all other groups, there were no positive circumferential, proximal, or distal surgical margins, and there was no significant difference between the groups (p>0.05). Macroperforation was positive in one patient in both Group 1 and Group 2 (1.72% and 3.57%, respectively), and there was no difference between the groups. The presence of perineural invasion, perivascular invasion, tumor deposits, and peritoneal invasion in Groups 1, 2, and 3 was as follows: 21 (36.2%), 8 (28.57%), 20 (50%); 27 (47.36%), 13 (46.42%), 21 (52.5%); 17 (29.82%), 7 (25%), 11 (27.5%); and 2 (3.5%), 3 (10.71%), 4 (10%), respectively. There was no statistically significant difference between the groups (p>0.05). When comparing pathological stages, the number of patients in Stages 1, 2, 3, and 4 for Groups 1, 2, and 3 were as follows: Stage 1: 2 (3.5%), 1 (3.57%), 0 (0%); Stage 2: 29 (50.87%), 17 (60.81%), 15 (37.5%); Stage 3: 20 (35.7%), 7 (25%), 19 (47.5%); Stage 4: 7 (12.28%), 3 (10.71%), 6 (15%). There was no statistically significant difference between the groups (p>0.05).

Table 3. Comparison of pathologic results between anatomic class

	Group 1 (n:57)	Group 2 (n:29)	Group 3 (n:40)
NHLN	19.6	16.1	13.6
Differentiation			
Grade 1	17 (29.82%)	11 (39.28%)	9 (22.5%)
Grade 2	29 (51.25%)	11 (39.28%)	20 (50%)
Grade 3	9 (15.78%)	5 (17.85%)	7 (17.50%)
Grade 4	3 (5.26%)	1 (3.57%)	4 (10%)
Surgical margin tumor			
Proximal	0	0	0
Distal	0	0	0
Circumpharantial	0	0	1 (2.5%)
Perineural invasion	21 (36.20%)	8 (28.57%)	20 (50%)
Perivascular invasion	27 (47.36%)	13 (46.42%)	21 (52.5%)
Tumor deposit	17 (29.82%)	7 (25%)	11 (27.50%)
Peritoneal invasion	2 (3.50%)	2 (10.71%)	4 (10%)
Patologic stage			
1	2 (3.50%)	1 (3.57%)	0
2	29 (50.87%)	17 (60.81%)	15 (37.50%)
3	20 (35.70%)	7 (25%)	19 (47.50%)
4	7 (12.28%)	3 (10.71%)	6 (15%)

DISCUSSION

When colon cancers are divided into proximal and distal or right and left colon cancers, it is known that proximal and distal colon cancers have different genetic, biological, and clinicopathological characteristics.[10-13] Transverse colon cancers, which are separated at the site where this distinction is made, have been reported to have a different course compared to other segments of the colon.[3,9] In this study, it was theoretically expected to find clinical and pathological differences between proximal and distal colon cancers, but no differences were found between the groups in both embryological and anatomical classifications.

Studies have shown that right colon cancers are generally associated with a worse prognosis than left colon cancers, regardless of the local stage of the tumor, as long as they are not metastatic.[14,15] These studies often attribute this difference to genetic and environmental factors. However, other studies have reported no significant differences when comparing the stages of right and left colon cancers, and the worse prognosis associated with right colon cancers may be due to the fact that they are often diagnosed at a later stage than left colon cancers.[16,17] Studies have also indicated an increasing frequency of right colon cancers in recent years, and one explanation for this is that right colon cancers are being diagnosed earlier. This may be attributed to increased awareness of colon cancer, more effective colonoscopy procedures, and the ability to remove adenomatous polyps, which are often found in the distal colon, through colonoscopic interventions.[18-20] In this study, no differences were found in the stages when transverse colon cancers were divided into proximal and distal. This may be attributed to increased awareness of colon cancer among both healthcare professionals and the public, as well as the increased use of colonoscopic, radiological, and laboratory-based screenings.

It is known that right and left colon cancers have different genetic and biological foundations.[16,21,22] In a study conducted by Lee, although there were genetic differences between right and left colon cancers, no significant differences in prognosis were observed in Stage 2 tumors, while in Stage 3 tumors, right colon tumors had a slightly worse prognosis.[22] However, in this study, no significant differences were found in the grades of tumors, and genetic differences were more associated with prognostic value through metastatic lymph nodes.[22] Another study by G.H. Lee highlighted these genetic differences and suggested that histologically more aggressive types (such as mucinous tumors) were more commonly associated with right colon cancers, rather than a direct relationship with tumor grade.[23] The biological behavior of tumors, as indicated by histomorphological features such as perineural invasion, perivascular invasion, and tumor deposits, is known to be associated with a worse prognosis. However, there have been no significant differences reported in tumor localization among these parameters.[23-26] Nevertheless, in a study by Pai, it was reported that the high incidence of BRAF and MMR gene mutations in right colon tumors led to increased lymphovascular and perineural invasion.[27] In this study, although numerical data showed that tumor grade and histopathological findings such as perineural and perivascular invasion were more common in proximal tumors, there were no statistically significant differences, which is consistent with the literature.

Lymph node dissection is an important step in colorectal cancer surgery, and it is recommended to remove at least 12 lymph nodes for surgical adequacy.[28,29] Webber's study even showed that patients who had more than 20 lymph nodes removed had higher five-year survival rates.[30] It has been reported that a greater number of adequate lymph nodes are removed after surgery in proximal colon tumors.[30-32] Yang's study suggested that in proximal colon cancers, the number of lymph nodes is more prognostic. The extent of lymph node dissection in the transverse colon is a topic of debate. Due to the proximity of the transverse colon to mesenteric lymph nodes, there can also be metastasis to extramesenteric lymph nodes.[9] Consistent with the literature, this study also found that more lymph nodes were removed in proximal colon cancers, although it was not statistically significant. Adequate numbers of lymph nodes were removed in all localizations and surgical procedures.

Study Limitation

The most significant limitation of the study is its retrospective nature, which may lead to potential errors and inaccuracies in the data. Additionally, the exclusion of patients due to missing information can be considered another limitation of the retrospective study. The small number of patients is also another obstacle in generalizing the findings.

CONCLUSION

When transverse colon cancers are classified embryologically and anatomically, no statistically significant differences were observed in parameters such as histological grade, lymph node count, perineural invasion, and perivascular invasion, similar to what is observed in proximal and distal colon cancers. However, hepatic corner and mid-transverse colon tumors nominally resemble proximal colon cancers.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ankara Bilkent City Hospital Ethics Committe (Date:19.06.2023, Decision No: E1-23-3693).

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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