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The Effect of Primary Tumour Resection on Prognosis in Emergency-operated Liver Metastatic Colon Cancer

Acil Ameliyat Edilen Karaciğer Metastatik Kolon Kanserinde; Primer Tümör Rezeksiyonun Prognoz Üzerine Etkisi

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ABSTRACT

Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths in western societies. It is also the third cause of cancer-related deaths in male and female populations in the world. In population-based studies, 25%-30% of CRC patients are faced with liver metastasis at some point in their disease. Colon and rectal cancers most frequently metastasise to the liver and lungs. This study, which was carried out in patients who were operated due to acute complications of liver metastatic CRC; aimed to investigate the effects of primary tumour removal on mortality, morbidity, and survival.

Methods: Patients with colon or rectal cancer with liver metastases who applied to the University of Health Sciences Turkey, İstanbul Training and Research Hospital Emergency Service between 2011 and 2016 and were urgently operated were included in the study.

Results: A total of 59 patients were evaluated. There were 30 (50.8%) male and 29 (49.2%) female patients. The ages of the participants ranged from 24 to 86 years, with a median age of 65 (24-86) years. Primary tumour resection was performed in 37 (62.7%) patients during emergency surgery, whereas resection was not performed in 22 (37.3%) patients. The postoperative survival of the patients is minimum 1 month and maximum 60 months. The files of patients with a survival of more than sixty months were not followed after the 60th month. Twenty-three patients never received chemotherapy and thirty-six patients were operated during chemotherapy treatment. The hospitalization period of 44 (74.6%) patients was more than 10 days, and the hospitalization period of 15 (25.4%) patients was 10 days or less. When we take 24 months as a basis for the survival of the patients, the number of patients with 24 months or more survival is 23 (39%) and the number of patients with survival below 24 months is 36 (61%). When the 24-month survival "cut off" value was taken, the independent data of the patients were evaluated individually in terms of prognosis and whether it was significant ($p>0.05$).

ÖZ

Amaç: Kolorektal kanser (CRC) batı toplumlarında kanser ile ilişkili ölümlerde en önde gelen sebeplerdendir ve dünyada kansere bağlı ölümlerin erkek ve kadında üçüncü nedenidir. Toplum bazlı çalışmalarda CRC hastalarının %25-30'u hastalıklarının bir döneminde karaciğer metastazı ile karşı karşıya kalmaktadır. Kolon ve rektum kanserleri en sık karaciğer ve akciğere metastaz yapmaktadır. Bu çalışmanın amacı karaciğer metastatik CRC'nin acil komplikasyonları nedeniyle ameliyat edilen hastalarda; primer tümörün çıkarılmasının mortalite, morbidite ve sürviye etkisini araştırmaktır.

Yöntemler: 2011-2016 yılları arasında Sağlık Bilimleri Üniversitesi, İstanbul Eğitim ve Araştırma Hastanesi Acil Servisi'ne başvuran karaciğer metastatik kolon veya rektum kanseri hastalarından acil ameliyat edilen hastalar çalışmaya dahil edilmiştir.

Bulgular: Toplam incelenen hasta sayısı 59'dur. Erkek hasta sayısı 30 (%50,8), kadın hasta sayısı 29'dur (%49,2). Minimum yaş 24 iken maksimum yaş 86 ve medyan yaş değeri 65'tir (24-86). Otuz yedi (%62,7) hastada acil operasyon sırasında primer tümör rezeksiyonu yapılırken, 22 (%37,3) hastada rezeksiyon yapılmamıştır. Hastaların operasyon sonrası yaşam süresi minimum 1 ay, maksimum 60 aydır. Altmış aydan fazla yaşam süresi olan hastaların dosya takibi 60. aydan sonra yapılmamıştır. Yirmi üç hasta hiç kemoterapi almamışken 36 hasta kemoterapi tedavisi sırasında ameliyat edilmiştir. Kırk dört (%74,6) hastanın hastanede yatış süresi 10 günden fazla iken 15 (%25,4) hastanın hastanede kalış süresi 10 gün ve daha azdır. Hastaların yaşam süresi için 24 ayı baz aldığımızda 24 ay ve üzeri survisi olan hasta sayısı 23 (%39) iken 24 ay altında survi süresi olan hasta sayısı 36 (%61)'dır. Yirmi dört aylık survi "cut off" değer alındığı zaman hastaların bağımsız verileri tek tek prognoz açısından 24 aya göre değerlendirilmiş ve anlamlı olup olmadığı incelenmiştir. Yaşam süresi 24 ay altı

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Conclusion: Metastatic CRC patients are generally in the advanced age group. Many of these patients also have additional pathologies. Performing primary tumour resection contributes significantly to the average life expectancy in urgently-operated metastatic CRC patients. Still, this is a difficult surgical procedure; the best decision should be made during surgery, with several factors such as the general condition of the patient, additional pathologies, the experience of the surgeon, and whether the tumour is resectable being taken into consideration.

Keywords: Colorectal cancer, metastasis, liver, survey

ve üstü olan grupta hastaların yaşları anlamlı (p>0,05) farklılık göstermemiştir.

Sonuç: Metastatik CRC hastaları genelde ileri yaş gurubundadır. Bu hastaların birçoğunda ek patolojiler de mevcuttur. Acil opere edilen metastatik CRC hastalarında primer tümör rezeksiyonu yapmak ortalama yaşam süresine anlamlı katkı sağlamaktadır. Yine de bu ameliyat zor bir operasyondur; hastanın genel durumu ek patolojileri cerrahın tecrübesi ve tümörün rezektabl olup olmaması gibi değişken faktörlerle en iyi karar ameliyat esnasında verilmelidir.

Anahtar Kelimeler: Kolon kanseri, metastaz, karaciğer, survi

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer-related death in western societies. It is also the third cause of cancer-related death in both male and female populations in the world (1). In population-based studies, 25%-30% of CRC patients are faced with liver metastasis at some point in their disease (2). Colon and rectal cancers most frequently metastasise to the liver and lungs (3). Haematogenous spread through the portal vein is most commonly affects the liver (4). Recent studies show an increase in liver metastasis in colon cancers in recent years (3). Despite all developments in the field of surgery and oncology, only 25% of patients with liver metastases of colon cancer (CRCLM) are cured (5). Only 10%-25% of CRC patients have a resectable liver metastases at the time of diagnosis (6). The only known cure for this patient group is oncological surgery. The order of surgical and oncological treatment in CRCLM patients correlated with: the size and number of liver metastases, the presence or not in both lobes, the residual liver volume after surgery, the presence or absence of other comorbidities. In addition, the order of treatment to be given is affected by ileus, bleeding, or perforation caused by colon cancer. Although there is no clear consensus on this multifactorial situation, many surgeons prefer short chemotherapy treatment if there are no emergencies such as ileus, bleeding, perforation etc for CRCLM patients, after which they proceed to the surgery. After primary tumour resection, if liver metastasis is not suitable for resection, the patient continues chemotherapy (7,8). In this study, we compared the prognosis of patients who were admitted to the emergency department with an acute complication of CRC requiring emergency surgery, such as intestinal obstruction, bleeding, and perforation with liver metastasis, who underwent primary tumour resection during emergency surgery and who were placed on chemotherapy without resection of the primary tumour.

Methods

Patients with colon or rectal cancer with liver metastases who visited the emergency service between 2011 and 2016 and were operated urgently were included in the study. The files of the patients were analysed retrospectively. Demographic data, performance or not of tumour resection, commencement or not of neo-adjuvant chemotherapy, duration of hospital stay, and post-operative survival were analysed. The first patient included in the study was operated in February 2011, the last patient was operated in November 2015, and the 5-year survival of the patients from the date of surgery was evaluated. The effects of the previously-mentioned independent data on prognosis were compared.

This study, which is a retrospective analysis of CRC patients, was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (decision no: 2420, date: 12.06.2020). Written informed consent was obtained from all cases.

Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, median, lowest value, highest value, frequency, and ratio values were used. The distribution of variables was measured by the Kolmogorov-Smirnov test. Mann-Whitney's U test was used to analyse quantitative independent data. The chi-square test was used in the analysis of qualitative independent data. Fischer's Exact test was used when the chi-square test conditions were not met. SPSS 26.0 software was used in the analysis.

Results

We evaluated 59 patients; 30 (50.8%) males and 29 (49.2%) females. The ages of the participants ranged from 24-86 years, with a median age of 65 (24-86) years. Primary tumour resection was performed in 37 (62.7%) patients during emergency surgery, whereas resection was not performed in 22 (37.3%) patients. The postoperative survival of the patients ranged from 1-60 months. Patients with a survival of more than 60 months were not followed up after the 60th month. While 23 patients never received chemotherapy, 36 were operated while they were on chemotherapy. The hospitalisation period of 44 (74.6%) patients was more than 10 days, while that of 15 (25.4%) patients was 10 days or less (Table 1). When we consider 24 months as the reference for the post-operative survival of the patients, the number of patients with a survival of 24 months or more is 23 (39%), while the number of patients with a survival below 24 months is 36 (61%). When the 24 month survival was taken as the cut-off value, the independent data of the patients were evaluated individually for 24 months in terms of prognosis and statistical significance was also determined.

There was no statistically significant difference (p>0.05) in the ages of the patients in the group with a survival of less than 24 months and that with survival over 24 months after surgery. The preoperative albumin value did not differ significantly (p>0.05) in the group with a survival of less than 24 months and that with survival over 24 months after surgery.

Primary tumour resection rate was significantly lower ($p<0.05$) in the group with a postoperative survival of ≤24 months than in the group with a postoperative survival of >24 months after surgery. The degree of tumour differentiation did not differ significantly ($p>0.05$) between the two groups. The neoadjuvant chemotherapy treatment rate did not differ significantly ($p>0.05$) between the two groups. The distribution of metastasis location did not differ significantly ($p>0.05$) between the two groups. The duration of hospitalisation did not differ significantly ($p>0.05$) between the two groups.

As seen in Table 2, the number of patients who lived for at least 24 months after operation was higher in the group in which primary tumour excision was performed. The ages of the patients did not significantly differ ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. There was no significant difference in gender distribution ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. The preoperative albumin value did not differ significantly ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. In the group with hospital stay was longer than 10 days, the survival time after surgery was significantly shorter ($p>0.05$) than that in the group with less than 10 days of hospital stay.

Primary tumour excision rate did not differ significantly ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. The neoadjuvant chemotherapy treatment ratio did not differ significantly ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. The distribution of metastasis location did not differ significantly ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days. The duration of hospitalisation did not differ significantly ($p>0.05$) between the group whose hospital stay was less 10 days and that whose hospital stay was more than 10 days (Table 3).

Discussion

CRC is the most common cancer of the gastrointestinal tract (9). It is the 3rd leading cause of mortality in men and women. In recent years, early diagnosis and risk management are possible with community screening programmes and advanced technological imaging methods (10). Despite all community screening programmes and advances in surgery and oncology, there is no significant reduction in the number of metastatic colon cancer patients. In 50%-60% of all CRC patients, liver metastasis will develop at some point in their lives (10,11).

The majority of CRCs are first diagnosed in emergency departments, where they present with acute complications of the disease such as intestinal obstruction, perforation and bleeding. These acute complications are often life-threatening emergencies and are managed through emergency surgery. The most important factors determining the prognosis after surgery are advanced age, existing comorbidities, and advanced tumour stage (12). However, whether or not intestinal obstruction is a sign of bad prognosis is controversial (13,14).

Table 1. Analysis of all patients' data

		Min-max	Median	Mean ± SD/n-%
Age		24.0-86.0	65.0	64.5±12.0
Gender	Female	-	-	29/49.2%
	Male	-	-	30/50.8%
Preop albumin		1.9-4.7	2.8	3.0±0.7
Survival after surgery, months		1.0-60.0	16.0	21.4±14.3
Primary tumour excision	(-)	-	-	22/37.3%
	(+)	-	-	37/62.7%
Tumour differentiation	Low	-	-	23/39.0%
	Moderate	-	-	23/39.0%
	Well	-	-	13/22.0%
Neoadjuvant chemotherapy treatment	(-)	-	-	36/61.0%
	(+)	-	-	23/39.0%
Liver metastasis location	Left	-	-	10/16.9%
	Right	-	-	30/50.8%
	Bilateral	-	-	19/32.2%
Duration of hospitalisation	≤10 days	-	-	15/25.4%
	>10 days	-	-	44/74.6%
Survival after surgery	≤24 months	-	-	36/61.0%
	>24 months	-	-	23/39.0%

SD: Standard deviation, min: minimum, max: maximum

Table 2. Analysis of patients' data according to postoperative survival

		Survival after surgery ≤24 months		Survival after surgery >24 months		p
		Mean ± SD/n-%	Median	Mean ± SD/n-%	Median	
Age		63.7±14.3	66.0	65.7±7.4	65.0	0.864[m]
Gender	Female	18/50%	-	11/47.8%	-	0.274[X²]
	Male	17/47.2%	-	13/56.5%	-	
Preop albumin		3.1±0.7	3.1	2.8±0.6	2.7	0.239[m]
Primary tumour excision	(-)	20/55.6%	-	2/8.7%	-	0.000[X²]
	(+)	16/44.4%		21/91.3%		
Tumour differentiation	Low	18/50.0%	-	5/21.7%	-	0.054[X²]
	Moderate	13/36.1%		10/43.5%		
	Well	5/13.9%		8/34.8%		
Neoadjuvant chemotherapy	(-)	22/61.1%	-	14/60.9%	-	0.985[X²]
	(+)	14/38.9%		9/39.1%		
Liver metastasis location	Left	5/13.9%	-	5/21.7%	-	0.735[X²]
	Right	19/52.8%		11/47.8%		
	Bilateral	12/33.3%		7/30.4%		
Hospitalisation	≤10 days	11/30.6%	-	4/17.4%	-	0.257[X²]
	>10 days	25/69.4%		19/82.6%		

[m]Mann-Whitney U test, [X²]chi-square (Fischer Exact test), SD: standard deviation

Table 3. Analysis of patients' data according to length of stay in hospital

		Hospitalisation ≤10 days		Hospitalisation >10 days		p
		Mean ± SD/n-%	Median	Mean ± SD/n-%	Median	
Age		59.5±15.7	64.0	66.2±10.2	66.0	0.864[m]
Gender	Female	15	-	14	-	1.000[X²]
	Male	14	-	16	-	
Preop albumin		3.3±0.6	3.4	2.9±0.7	2.6	0.239[m]
Survival after surgery months		16.3±7.0	15.0	23.1±15.7	22.5	0.000[m]
Primary tumour excision	(-)	6/40.0%	-	16/36.4%	-	0.801[X²]
	(+)	9/60.0%	-	28/63.6%	-	
Tumour differentiation	Low	6/40.0%	-	17/38.6%	-	0.606[X²]
	Moderate	7/46.7%	-	16/36.4%	-	
	Well	2/13.3%	-	11/25.0%	-	
Neo-adjuvant chemotherapy	(-)	11/73.3%	-	25/56.8%	-	0.257[X²]
	(+)	4/26.7%	-	19/43.2%	-	

[m]Mann-Whitney U test, [X²]chi-square test (Fischer Exact test), SD: standard deviation

In a study by Ergun et al. (10), 252 patients with metastatic colon cancer were evaluated in terms of primary tumour resection, and demonstrated that performing primary tumour resection before chemotherapy has no survival benefit. As a result, they reported that it would be more appropriate to start treatment with chemotherapy and biological agents in asymptomatic metastatic patients, thus, they showed that patients would be affected less by the mortality and morbidity of the operation.

In a study by de Mestier et al. (15), primary tumour resection and immediate subsequent chemotherapy in patients with asymptomatic metastatic CRC was found to be superior in terms of the duration and quality of postoperative survival of the patients compared to chemotherapy alone. Louis recommends primary tumour resection in patients under the age of 70 who: do not have extrahepatic metastases, have less than two metastases in the liver, and have at least half of the liver intact without metastasis (15).

Simillis et al. (16) found that performing primary tumour resection and then initiating chemotherapy in patients with asymptomatic metastatic CRC was superior in terms of survival compared to direct chemotherapy in a large meta-analysis with 77 studies they examined (16). Nevertheless, they suggested starting with primary tumour resection in a multidisciplinary manner. They examined the patients in six groups and the average life expectancy of the group that did not receive any treatment was found to be 4.02 months. The mean life expectancy was 7.42 months in the group in which primary tumour resection

was performed and did not receive chemotherapy. In the groups that received chemotherapy and bevacizumab without primary tumour resection, the mean survival time was 14.3 months and 17.27 months, respectively. The mean survival was 21.52 months and 27.52 months in two separate groups in which primary tumour resection was performed and immediately followed by chemotherapy and bevacizumab, respectively (16). The results of this meta-analysis partially support the findings of our study.

As above, the number of such studies can be increased, and there are studies that suggest direct chemotherapy before primary tumour resection. The difference between our study and these studies is that patients had emergency surgery as a result of symptoms associated with the primary tumour and to compare whether to perform primary tumour resection during surgery.

CRCLM patients after or before diagnosis: It is a patient group with a high probability of emergency surgery due to reasons such as ileus, bleeding, and perforation. Performing primary tumour resection during emergency surgery might result in a longer hospital stay, a higher rate of mortality and morbidity and this delays in the patient's commencement of chemotherapy. In our study, there was no significant difference in terms of hospital stay between the group that underwent primary tumour resection and the group that did not. The survival time after surgery was significantly more in the primary tumour resection group.

Conclusion

Metastatic CRC patients are generally in the elderly population. Many of these patients also have additional comorbidities. Performing primary tumour resection contributes significantly to the average life expectancy in urgently-operated metastatic CRC patients. Still, this is a difficult surgical procedure. The best decision should be made during surgery, with several factors such as the general condition of the patient, additional comorbidities, the experience of the surgeon, and the resectability of the tumour being taken into consideration.

Ethics

Ethics Committee Approval: This study, which is a retrospective analysis of CRC patients, was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (decision no: 2420, date:12.06.2020).

Informed Consent: Written informed consent was obtained from all cases.

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