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Influence of the Type and Amount of Liver Resection on the Survival of the Patients with Colorectal Metastases

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Abstract

INTRODUCTION: Colorectal liver metastases have a poor prognosis, and only 2% have an average 5-year survival if left untreated. Despite radical resection, the average five-year survival is between 25% and 44%.

AIM: To explore the experience of the Clinic in the treatment of colorectal liver metastases, comparing it with data from the literature and based on the comparison to determine the influence of the type and extensity of resection survival after radical surgical treatment of patients.

METHODS: This is a retrospective study. The study comprised the period between 01.01.2006 to 31.12.2015. It included a total of 239 cases, of whom: 179 patients underwent radical interventions, 5 palliative and 55 patients underwent explorative interventions due to liver metastases.

RESULTS: Radical resection of liver metastases has the impact of the patient survival, and the survival is the smallest in the patients with left hemihepatectomy and the longest in the patients with bisegmentectomy. But no specific technique and the number of resected segments influenced the survival of patients with colorectal liver metastases.

CONCLUSION: In patients with colorectal liver metastases only resection has potentially curative character. The type and amount of liver resection has no influence of the survival.

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide after lung cancer and breast cancer [1] [2]. A large percentage of 50-70% of patients develops colorectal liver metastases (CRLM) because of hematogenous dissemination of primary cancer [3] [4] [5] [6] [7]. Synchronous metastases are diagnosed in 15-25% [8] [9] [10] during the primary diagnosis of CRC and in 20-25% [11] [12] [13] [14] [15] in the first five years metachronous metastases develop. They represent the most common cause of death so that 77% of untreated patients die in the first year, and only 14-23% survive more than three years [16] [17] [18] [19]. Surgical resection represents the only curative treatment approach to patients with CRLM; in larger series patients treated with resection have a mean 5-year survival from 25% to 44% [15] [20] [21], but only 15-25% [22] of metastasis of liver are initially resectable. Poor prognosis of the disease is the cause of looking for opportunities to improve postoperative results which correspond with defining determinants of survival.

To explore our experience in the treatment of colorectal liver metastases (CRLM), comparing them with data from the literature, and based on the comparison to determine the influence of type and amount of resection of the survival after radical surgical treatment of patients.

Material and Methods

A retrospective study was conducted at the Clinic of General and Hepato-pancreatic surgery at the University Hospital "Aleksandrovska" – Sofia, Bulgaria. The study comprised the period between 01.01.2006 to 31.12.2015. It included a total of 239 patients, of whom: 179 patients (74.9%) underwent radical interventions (atypical resection - 57, resection of 2 segments - 24, resection of 3 segments - 18, resection of >3 segments - 10, left lobectomy - 15, left hemihepatectomy - 4, right hemihepatectomy - 12, metastasectomy - 20, resection with another procedure - 19, atypical resection and metastasectomy - 9, left lobectomy and atypical resection - 5, atypical resection and alcoholization - 1, atypical resection and thermoablation - 4; and 5 palliative and 55 patients underwent explorative interventions due to liver metastases (biopsy - 55, biopsy and biliary drainage - 2, thermoablation - 1, alcoholization - 2). Also, 119 (49.8%) patients were diagnosed with synchronous metastases, 120 (50.2%) patients with metachronous metastases, including 7 (2.9%) with metachronous metastases with recurrence on the colon.

The follow-up period of the patients operated on for colorectal liver metastases in the Clinic was 5 years after resection of the liver.

The study included all patients with liver metastases from colorectal cancer regardless of their age and gender;

The study included all patients with liver metastases from colorectal cancer: synchronous metastases, metachronous metastases and metastases appearing with local recurrence of cancer;

The endpoints were to determine the following:

1. Survival depending on the type of surgical intervention: radical surgery or the palliative surgery or biopsy;

2. Cumulative overall survival depending on the type of the surgical intervention: radical surgery or the palliative surgery or biopsy;

3. To assess whether the specific type of radical hepatic resection has an influence on mortality (atypical resection, 2 - segment resection, resection of more than 3 segments, left - lobectomy, left hemihepatectomy, right hemihepatectomy, metastasectomy, combined liver surgery) as well as on median survival;

4. To assess whether the specific type of palliative intervention (biopsy, thermoablation, alcoholization) has an influence on mortality as well as on survival;

5. To assess whether the volume of liver resection (small and large resection) has an influence on mortality as well as on median survival.

Statistical analysis of the collected material to determine the factors for survival was done using the SPSS-19 statistical program.

Results

The average survival of patients undergoing radical intervention is about three times longer than that of palliative care. The Logging and Breslow statistical tests, as well as the regression analysis, confirm that the type of operative intervention involved is a significant factor in the survival of patients with this pathology (Figure 1).

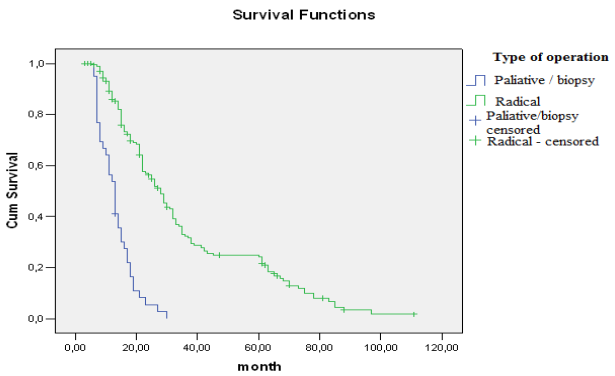

Figure 1: Survival curves depending on the type of surgical intervention; Log Rank (Mantel-Cox) p < 0.0001; Breslow p < 0.0001

Patients undergoing radical surgery are associated with a 79.7% lower risk of lethal outcome than patients with palliative care or patients who underwent biopsy (Table 1, 2).

Table 1: Cumulative overall survival depending on the type of the surgical intervention

Type of operation	Deaths	Cumulative survival % (Std.Error)		
	N (%)	1-year	3-year	5-year
Radical	131 (78.44)	89.2 (0.028)	32.4 (0.04)	24.1 (0.03)
Palliative / biopsy	38 (92.68)	53.8 (0.08)	0	0

To assess whether the specific volume and type of radical hepatic resection influence survival, we analysed the data from the patients we follow.

Table 2: Cox regression analysis according to the applied surgical intervention

	p	Exp (B)	95% CI for Exp (B)
Reference category-palliative intervention/biopsy			
Radical intervention	<0.0001	0.203	0.135-0.306

The distribution of established deaths for

patients over the study period treated with radical surgery depending on the type of resection is as follows: - 64.15% mortality in patients with atypical resection (34/53 patients); - 68.18% in the 2-segment resection group (15/22 patients); - 100% mortality was recorded in resection of more than 3 segments (8/8 patients); - 86.67% of left-lobectomy patients died in the follow-up (13/15 patients); - 100% of those with left hemi-hepatectomy (3/3 patients); - 91.67% of patients with right hemi-hepatectomy (11/12 patients) and 85% of cases with metastasectomy (17/20 patients).

In patients undergoing combined liver surgery, 83.33% of the patients were with fatal outcome.

Survival analysis revealed that median survival was lowest in the left hemi-hepatectomy group (about 14 months), and the highest in patients with two-segment resection (48 months).

Table 3: Mean and median survival based on the type of liver resection applied

Type of resection	Mean and median survival					
	Mean	Std.err	95% CI	Median	Std.err	95% CI
Atypical resection	40.565	4.026	32.675-48.456	35.0	6.525	22.211-47.789
Resection of 2 segments	48.229	7.39	33.744-62.714	36.0	11.38	13.69-58.31
Resection of 3 segments	28.125	5.204	17.924-38.326	22.0	14.0	0.000-49.44
Resection of more than 3 segments	31.125	7.391	16.639-45.611	28.0	11.314	5.825-50.175
Left lobectomy	32.214	5.451	21.53-42.898	26.0	1.852	22.371-29.629
Left hemi-hepatectomy	13.667	1.333	11.053-16.28	15.0	0.0	
Right hemi-hepatectomy	24.476	2.455	19.665-29.287	22.0	3.143	15.839-28.161
Metastasectomy	40.047	7.076	26.178-53.915	32.0	8.876	14.603-49.397
Resection + other procedure	26.063	4.093	18.041-34.085	26.0	2.91	20.297-31.703

This difference is statistically significant (P = 0.004, P = 0.043), but when comparing all methods used, no "best" surgical method for treating CRLMs (Table 3, Figure 2).

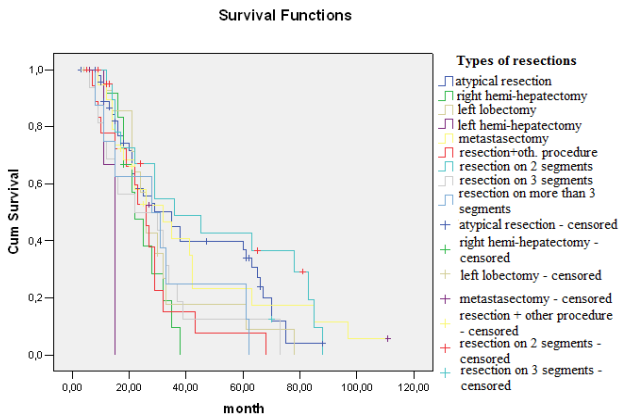

*Figure 2: Survival curves depending on the type of resection; Log Rank (Mantel-Cox) P = 0.004**; Breslow P = 0.043*; *P < 0.05; **P < 0.01*

In regression analysis, none of the operative techniques showed an advantage as a predictor of survival (Table 4).

Table 4: Cox regression analysis according to the type of liver resection applied

Type of resection	p	Exp (B)	95% CI for Exp (B)
Reference category – other types of resection			
Atypical resection	0.237	0.788	0.531-1.169
Resection of 2 segments	0.053	0.583	0.337-1.006
Resection of 3 segments	0.28	1.348	0.784-2.316
Resection of more than 3 segments	0.378	1.383	0.673-2.839
Left lobectomy	0.524	1.206	0.678-2.147
Right hemi-hepatectomy	0.114	1.661	0.885-3.116
metastasectomy	0.299	0.755	0.444-1.284
Resection + other procedure	0.113	1.555	0.901-2.685

The mortality analysis after a palliative intervention or biopsy showed that in this group the mortality was 94.87% of the patients. Only the patient who has been subjected to thermoablation is alive from the group of palliative patients. The Kaplan-Meier method of survival was examined according to the type of palliative intervention performed in figure 3.

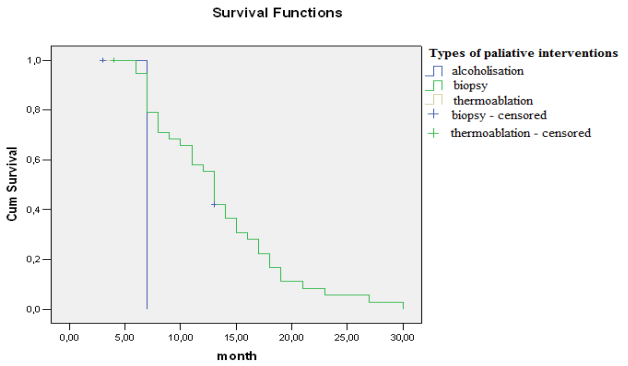

Figure 3: Survival curves depending on the type of palliative intervention

As can be seen from the graph and the additional regression analysis (Table 5), the application of biopsy or palliative intervention due to the inability to perform a radical intervention in CRLM patients significantly degrades long-term treatment outcomes. The fact that adjuvant therapy has been administered in most of these patients, and yet the average survival rate is significantly lower than that of the radically-operated patients, again proves the key role of surgical resection in the treatment of these patients.

Table 5: Cox regression analysis using palliative methods of treatment

Type of palliative operations	p	Exp (B)	95% CI for Exp (B)
Reference category-other palliative interventions			
Biopsy	0.153	0.22	0.027-1.756

Survival analysis was also performed according to the volume of surgery. In the group of patients undergoing large liver resection, 87 people (78.38%) died on long-term follow-up.

Table 6: Mean and median survival based on the volume of liver resection

Volume of the operation	Mean and median survival					
	Mean	Std.err	95% CI	Median	Std.err	95% CI
Big	31.042	2.043	27.037-35.047	26.0	1.84	22.393-29.607
Small	31.283	3.078	25.249-37.316	18.0	1.515	15.03-20.97

A fatal outcome was found in 82 (84.54%) patients with a small volume of hepatic intervention. The average survival in both groups is about 31 months (Table 6, Figure 4).

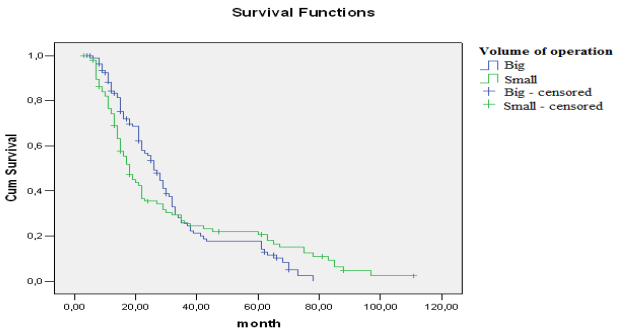

Figure 4: Survival curves depending on the volume of liver resection; Log Rank (Mantel-Cox) P = 0.796; Breslow P = 0.12

The additional analysis of the results (Cox regression) did not establish a significant correlation between the volume of surgical intervention according to the number of resected liver segments and the survival in patients with CRLM (Table 7).

Table 7: Cox regression analysis (Univariate analysis) concerning the volume of liver resection

Volume of operation	p	Exp (B)	95% CI for Exp (B)
Reference category-Big			
small	0.8	1.041	0.762-1.424

Discussion

This retrospective study showed a significant difference in the survival of patients operated radically. Survival of patients OS operated with non-anatomical resection NAR is no different from the survival of patients treated with AR. Also, the difference in patient survival is identified as significantly larger in the group of small resections, but this does not set the number of resected segments as a survival factor. Anatomical resection provides better cleaning between tumor deposits and the liver transaction line and is recommended as a standard procedure for metastatic liver tumor [24]. Non-anatomical resection is useful in small metastases, with little risk of microscopic local invasion [23]. Non-anatomical resection NAR has become more commonly used in view of the possibility of storing a larger volume of hepatic parenchyma, but the NAR compared to AR is associated with a higher incidence of positive resection ranges (R1 resection) [25]. Consensus has been widely accepted that a positive surgical margin is a powerful predictor of patient survival and recurrence [32] [33] [34]. As has been reported, the rate for five-year survival ranges only from 17.1% to 20% for patients with positive margins compared with that ranging from 37% to 63.8% with negative margins [32] [33]. As to median survival, the median length was 23 months for patients with positive margins, less than 45 months with negative margins [33]. Besides, overall recurrence rates were significantly different between patients with positive margins and with negative margins (51.1% and 38.6%, respectively) [33]. Studies show that the type of resection (anatomic or non-anatomic) is irrelevant for postoperative morbidity and mortality, with both negative histological margins (R0 resection) being achieved [25] [26] [27] [28] [29]. The use of non-anatomical resection has certain advantages such as lower blood loss, significant shorter operating times and shorter duration of hospital treatment [25] [26] [28]. As previously reported [35] [36] [37], AR featuring higher level of surgical technique difficulty would often be associated with longer operation duration and more liver parenchyma loss. Bile leakage, wound infection and intra-abdominal collections constituting the major types of complications all show evident preferences to AR group over NAR group. Taken together, AR might promote the incidence of postoperative morbidity. The main cause for the inferiority of AR to NAR in terms of mortality is thought to be its larger loss of liver parenchyma. With more extensive parenchymal resection, AR would consequently carry a more substantial risk. As reported by Lalmahomed ZS [28], postoperative hepatic failure resulting from insufficiency of liver remnant was the primary cause of mortality in AR group. But the type of resection of the liver does not affect the survival of patients with CRLMs.

Zorzi et al., [26] report a 5-year survival rate of 61% in favour of the NAR and 60% in the case of AR. Guzzetti et al., [30] -5-year survival of 29% for the NAR and 27% for AR. Many studies find that the type and extensity of the resection don't influence the survival, but blood loss is crucial as a factor of postoperative morbidity and mortality [31]. Also, other factors of survival such a type, number, size, and localisation correspond with the type and the extensity of resection of liver and also have the implication of long-term survival. To conclude that the patients treated with NAR and AR have similar OS survival of the patients with colorectal liver metastases. Also, the amount of the liver resection sometimes is crucial for the surgical strategy, and it has implications for the postoperative morbidity and mortality, but it isn't a factor of long-term survival.

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