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Advanced age; not a contraindiction for resections of colorectal liver metastasis recurrence

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ABSTRACT

Aim: The influence of advanced age on the outcome of repeat resections performed for colorectal liver metastasis (CLM) is ill-defined. We aimed to evaluate the safety and efficacy of repeat resections performed for the recurrence of CLMs in younger (≤70 years) and elderly patients (70< years), and to define predictive factors of survival.

Material and Method: A prospectively maintained database of a single center including 291 CLM patients between 1998 and 2019 was analyzed retrospectively. Short and long-term outcomes were compared among younger (n=99, 34%) and elderly (n=192, 66%) patient groups who were treated by repeat resections for CLM recurrence.

Results: Although statistically not significant, analysis of different age groups (≤70, 70-75, 75-80, and 80< years) have given similar results in terms of 1, 3, and 5-year survival (p=0.143). Globally curative resection was validated as a determinant factor in the estimation of survival following resections performed for recurrences according to multivariate analysis (p<0.05).

Conclusion: Repeat resections for the recurrence of CLMs in selected elderly patients are reliable with regards to similar survival outcomes achieved compared to their younger counterparts.

Keywords: Colorectal liver metastasis (CLM), liver recurrence, resection, elderly patients

INTRODUCTION

Colorectal cancer (CC) stands for the third most common cancer worldwide and the liver is the most common site of distant organ metastasis with an approximate rate of 35-58% (1-3). Surgery with curative intent is the best treatment option with an average 25-58% rate of 5-year survival (4-6).

Around 60% of the patients experience liver recurrences despite previously done curative-intent resections. Five-year survival rates following resections performed for liver recurrences are 21-88% (7-10). Improvements in treatment methods and growing experience have enabled surgeons to be more confident while performing surgery, and thus have encouraged to perform multiple resections.

Advanced age is one of the main concerns in deciding to perform liver surgery due to the increased risk of certain perioperative complications (11). This becomes more complicated when it is a redo surgery since re-resections are technically more challenging due to the adhesions of the previous surgery, and the liver is prone to bleeding due to increased fragility. Therefore, the management of repeat liver resections in elderly patients demands extra effort and attention to provide certain benefit.

We aimed to analyze and compare short and long-term outcomes following repeat liver resections among younger (≤70 years) and elderly (70< years) patients. The secondary end-point was to define predictive factors of survival after recurrence.

MATERIAL AND METHOD

The study was carried out with the permission of Istanbul Göztepe Prof. Dr. Süleyman Yalçın City Hospital Clinical Researches Ethics Committee (Date: 22.02.2023, Decision No: 2023/0124). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Consecutive patients who were treated at 'Centre Hépato-Biliaire, Paul Brousse Hospital, Villejuif, France,' between 1998 and 2019 were investigated. Relevant ones with a history of resection due to the recurrence of CLM were considered for further analysis. The patients who were managed non-surgically (Transarterial Embolization (TAE), Transarterial Chemoembolization (TACE), Radiofrequency Ablation (RFA), Microwave Ablation

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(MWA), SIRT (Selective internal radiation therapy)) or resected by Two-stage Hepatectomy (TSH) or ALLPS (Associated Liver Partition Portal Vein Ligation and Staged-Hepatectomy) were excluded.

Short and long-term outcomes of younger and elderly patients were compared with each other in terms of clinical characteristics, operative, and histopathological features, disease-free (DFS), and overall survival (OS). Different aged groups (≤70, 70-75, 75-80, and 80<years) were compared with each other in terms of 1, 3, and 5-year OS. Obtained results were analyzed to define predictive factors of survival after recurrence.

The terminology used to define the extent of resections was selected according to 'Brisbane Guidelines 2000'. Liver resections that were classified as 'major' represented those with equal to or more than three segments, and the 'limited' resections stated the ones less than three segments.

Preoperative Evaluation and Patient Selection

Included patients were selected from those that were under routine follow-up after initial resections performed for CLM. Detailed evaluations (Abdominopelvic ultrasound (US), computerized tomography (CT), magnetic resonance imagining (MRI), and positron emission tomography (PET) scans, measurement of tumor markers (CEA (Carcinoembryonic antigen) and CA 19-9)) revealed the ones with intra and extra-hepatic recurrences, and also ensured to choose the ones that were feasible for repeat resections.

Those who were considered for surgery were preoperatively evaluated in detail during multi-disciplinary meetings counting in the technically demanding nature of resections because of possible adhesions, increased fragility of the liver due to previous chemotherapy and surgery, advanced age, and associated co-morbidities.

Response to neoadjuvant therapy was determined by CEA levels, radiological assessments on control scans, and histopathological evaluations according to tumor regression grade (TRG) (12). Responses were graded according to a scoring scale between '0' and '5', which the minimum grade ('0') defining the term 'non-assessable, and with an increasing rate of response as the maximum grade ('5') representing the complete response to treatment.

The ones with estimated insufficient future liver remnant (less than 30-40% postoperative remnant liver volume), extra-hepatic site involvement that would not be amenable for curative-intent resection, major vascular proximity, multi nodularity, and large tumor size were treated by preoperative chemotherapy.

Operational Characteristics

Whole abdominal exploration was performed routinely to look for extra-hepatic disease. Afterward, a bi-manual examination and US evaluation of the liver were performed accordingly. Different types of resections (Anatomic or non-anatomic) were selected to achieve complete tumor removal. Patients that would not have sufficient postoperative liver volume were treated with PVE (Portal vein embolization) before the operation to achieve adequate liver hypertrophy. Choice of vascular occlusions (None, selective, total, exclusion) was taken according to the type of resections. Ultrasonic dissectors, intra-operative US, argon beam, and bipolar forceps were used to facilitate the parenchymal dissections as much as possible.

Postoperative Follow-up and O

Postoperative follow-up was accomplished by physical examination, measurement of tumor markers (CEA, CA 19-9), the hepatobiliary US at 1st and every 4 months consecutively; and chest, and abdominal CT scans were performed every 8 months. Postoperative follow-up findings were evaluated based on the type and frequency of complications, and survival outcomes. The severity of complications was assessed according to the 'Dindo-Clavien classification (13).

Study end-points

The primary end-point was to assess repeat liver resections in elderly patients in terms of clinical outcomes when compared to the younger patients. The secondary end-point was to search for clinically relevant parameters, if any, estimating survival outcomes.

Statistical Analysis

The clinical characteristics of the research sample were compared using the x2 tests. For examining the survival probabilities of the patients, the log-rank test of the Kaplan-Meier method was used and compared according to variable factors. Lastly, a univariate analysis was performed among the research sample to identify independent prognostic factors of survival. In the context of research, $p \leq 0.05$ was considered statistically significant. Multivariate analysis was performed to define independent predictive factors of survival for factors with $p \leq 0.1$ in univariate analysis. Statistical analysis of the research was performed using SPSS® version 25.0 (IBM, Armonk, New York, USA).

RESULTS

Between 1998 and 2019, 443 patients were diagnosed with liver recurrence of CLM. Those with history of resection (n=291 (65.7%)) were included in the study, 152 (34.3%) ((n=141; not found eligible for surgery due to the advanced disease or the comorbid conditions) (n=11; missing data)) were excluded from further analysis (**Figure 1**).

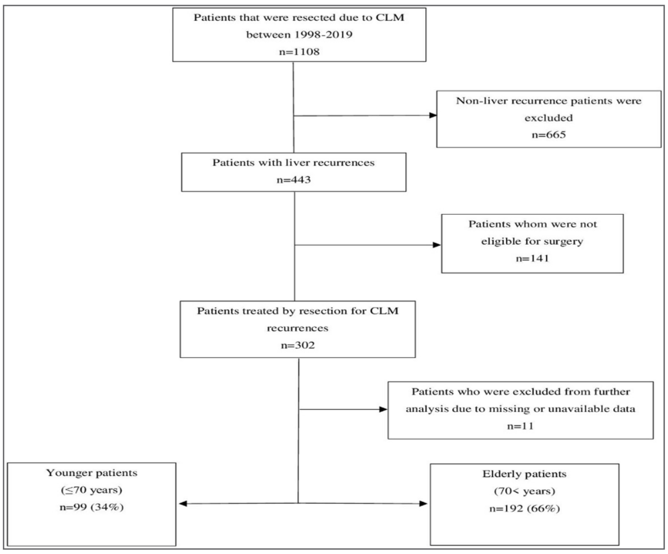

Figure 1. Flow chart

Comparison of Younger and Elderly Groups

The majority of the study population consisted of elderly patients (70< years) (n=192, 66%), and the less were the younger group (≤70 years) (n=99, 34%). The maximum diameter of resected lesions was mostly smaller than 50 mm ((≤70 years; 88.9%) vs (70< years; 83.3%)) (p=0.206). Resections were often limited which involved less than 3 segments for both age groups ((≤70 years; 65.7%) vs (70< years; 66.7%)) (p=0.863). Globally curative resections were achieved substantially in both groups ((≤70 years; 73.7%) vs (70< years; 74%)) (p=0.968). Demonstrations of all clinical characteristics are outlined in **Table 1**.

Of note; younger and elderly patients who were not eligible for resection had no significant differences in terms of tumor characteristics (Tumor size, number, location (lobar/bilobar), extra-hepatic extension), and survival outcomes.

Operative Characteristics

The time interval between initial and secondary resections (performed for recurrence) was longer in elderly patients ((≤70 years; 46.6 months) vs (70< years; 74 months)) (p=0.309). The majority of the patients in both groups were not treated with PVE preoperatively ((≤70 years; 87.9%) vs (70< years; 83.3%)) (p=0.305). Non-anatomic resections were selected more than anatomic and combined (anatomic and non-anatomic simultaneously) resections ((≤70 years; 40.2%) vs (70< years; 39.1%)) (p=0.615). Total pedicular occlusion or intermittent 'Pringle maneuver' was the commonly preferred approach with percentages of 61.6 vs 49.7 for younger and elderly patients in consecutive order (**Table 2**).

Complete necrosis and fibrosis were the dominant histopathological features recorded during microscopic evaluations of resected specimens in both groups (**Table 2**).

Table 1. Comparison of clinical characteristics

	Patients aged ≤70 years (n=99)	Patients aged 70< years (n=192)	P§
Sex			0.256
Male	70 (70.7)	123 (64.1)	
Female	29 (29.3)	69 (35.9)	
Primary tumour			0.723
Colon	75 (75.8)	149 (77.6)	
Rectum	24 (24.2)	43 (22.4)	
Liver metastases at diagnosis			0.191
No. of metastases			
1–3	78 (78.8)	163 (84.9)	
> 3	21 (21.2)	29 (15.1)	
Maximum diameter (mm)			0.206
0–50	88 (88.9)	160 (83.3)	
> 50	11 (11.1)	32 (16.7)	
Location			0.42
Unilateral	43 (43.4)	74 (38.5)	
Bilateral	56 (56.6)	118 (61.5)	
Hepatic resection			0.863
Type of resection			
Limited (< 3 segments)	65 (65.7)	128 (66.7)	
Major (≥ 3 segments)	34 (34.3)	64 (33.3)	
Liver curative resection			0.338
Yes	83 (83.8)	152 (79.2)	
No	16 (16.2)	40 (13.7)	
Globally curative resection			0.968
Yes	73 (73.7)	142 (74.0)	
No	26 (26.3)	50 (26.0)	
Combined treatment modalities to improve resectability			0.349
Yes	14 (14.1)	20 (10.4)	
No	85 (85.9)	172 (89.6)	
Concomitant extrahepatic disease			0.909
Yes	17 (17.2)	34 (17.7)	
No	82 (82.8)	158 (82.3)	
Preoperative chemotherapy			0.484
Yes	68 (68.7)	124 (64.6)	
No	31 (31.3)	68 (35.4)	
Clinical response to last line			0.334
Complete response	5 (10.2)	5 (3.9)	
Partial response	4 (8.2)	15 (11.8)	
Stabilization	13 (26.5)	29 (22.8)	
Disease progression	8 (16.3)	23 (18.1)	
Non-assessable	19 (38.8)	55 (43.3)	
Total no. of cycles			0.081
≤ 6	32 (65.3)	64 (50.4)	
> 6	17 (34.7)	63 ((49.6)	
Postoperative chemotherapy			0.923
Yes	52 (52.5)	102 (53.1)	
No	47 (47.5)	90 (46.9)	

Table 2. Operative and histopathological features

	Patients aged ≤70 years (n=99)	Patients aged 70< years (n=192)	P§
Time interval between operations (months)*	46.6 (189.5)	74 (258.6)	0.309
PVE			0.305
Yes	12 (12.1)	32 (16.7)	
No	87 (87.9)	160 (83.3)	
Type of resection			0.615
Anatomical	19 (20.7)	45 (25.9)	
Non-anatomical	37 (40.2)	68 (39.1)	
Combined	36 (39.1)	61 (35.1)	
Vascular occlusion			0.208
None	14 (19.2)	46 (30.1)	
Selective	6 (8.2)	16 (10.5)	
Total pedicular	45 (61.6)	76 (49.7)	
Vascular exclusion	8 (11)	15 (9.8)	
Intraoperative transfused blood units*	0.6 (1.6)	1.3 (3.5)	0.100
90-day postoperative complications			0.312
Yes	35 (35.4)	61 (31.7)	
No	64 (64.6)	131 (68.3)	
Grade of complications			0.651
0	64 (64.6)	131 (68.3)	
I	3 (3)	2 (1)	
II	16 (16.2)	32 (16.7)	
III	16 (16.2)	26 (13.5)	
IV	0 (0)	1 (0.5)	
Minimal margin of resection	2.7 (5.2)	3.1 (6.5)	0.621
Complete necrosis			0.635
Yes	3 (3)	6 (3.1)	
No	96 (97)	186 (96.9)	
Fibrosis			0.175
Yes	13 (13.1)	17 (8.9)	
No	86 (86.9)	175 (91.1)	
Histology of non tumoral liver			0.363
Normal	19 (28.4)	40 (32)	
Abnormal	48 (71.6)	85 (68)	
Histology of non tumoral liver			0.529
Normal parencymal architecture	52 (60.5)	114 (65.5)	
Congestion	0 (0)	1 (0.6)	
Fibrosis	8 (9.3)	22 (12.6)	
Noduler Hyperlasia	4 (4.7)	3 (1.7)	
Steatosis	18 (20.9)	27 (15.5)	
Other	4 (4.7)	7 (4)	
Last patient status			0.088
Alive	67 (67.6)	110 (57.2)	
Deceased	15 (15.1)	62 (32.2)	
Lost to follow-up	17 (17.1)	20 (10.4)	

Postoperative Morbidity and Mortality

Sixty-four (64.6%) patients in the younger group and 131 (68.3%) in the elderly group didn't have any postoperative complications before discharge. Only 1 (0.5%) patient in the elderly group had grade IV (According to 'Dindo-Clavien classification) complication which was due to liver insufficiency. Postoperative complications were mostly graded II-III in both younger (grade II:16.2% vs grade III:16.2%) and elderly groups (grade II:16.7% vs grade III:13.5%) respectively. Three (3%) patients in the younger group and 2 (1%) in the elderly group had grade I postoperative complications (p=0.651). There was no incidence of mortality recorded for both groups within 90-day postoperative follow-up.

Survival Analysis

Survival analysis of age groups demonstrated similar results for up to 4 years; 73.5%, 73.8%, 73.3%, and 73.3% for those aged ≤70, 70-75, 75-80, and 80< years respectively (p<0.001) (**Figure 2**).

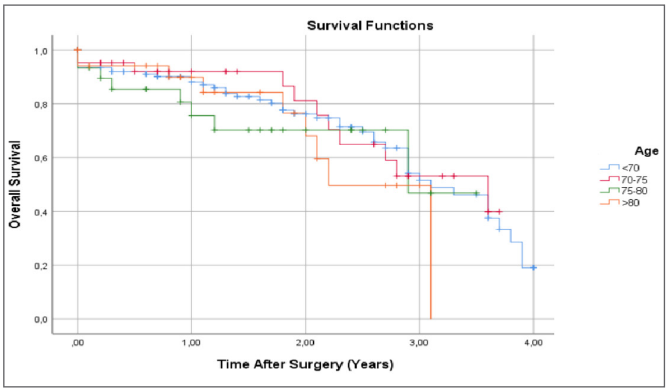

Figure 2. Overall survival according to different age groups (p<0,001 (log rank test))

Predictive Factors of Postoperative Survival

Variances in the origin of tumors according to locations on colon vs rectal didn't show superiority among each other in terms of survival considering 1, 3, and 5-year follow-up (p=0.138) (**Table 3**). The number of liver metastasis had similar impact on survival outcomes among younger and elderly age groups. Differences in tumor diameters (50 mm> vs >50 mm) didn't reach a significant result considering 1, 3, and 5-year survival analysis (p=0.313). Unilobar or bilobar tumoral involvement didn't have an influential role in survival among the study group (**Table 3**). Responses given to chemotherapy have shown marked differences in terms of survival (1, 3, 5-year); such that patients having a complete and partial response to chemotherapy had a clear advantage of survival, particularly for up to 3-year follow-up compared to other groups including stable response, and disease-progression groups (p=0,055).

Table 3. Clinical impact of prognostic factors on 1, 3, and 5-year survival

	No of Patients	1 Year Survival	3 Year Survival	5 Year Survival	P§
Sex					0,223
Male	193	76.9	59.9	40.3	
Female	98	76.4	62.7	48.2	
Age					0.143
<70	185	75	69.5	44.1	
70-75	42	79.3	61.7	37.9	
75-80	30	85	64.3	55	
80<	34	72	60	48	
Primary tumour					0.138
Colon	224	75.3	60.6	51.8	
Rectum	67	78.8	61.5	47.7	
Liver metastases at diagnosis					
No. of metastases					0.212
1–3	241	75.1	61.1	42.4	
> 3	50	81.1	59.5	46.8	
Maximum diameter (mm)					0.313
0–50	248	74.6	60	41.4	
> 50	43	83.8	64.9	40.8	
Location					0.058
Unilateral	117	71.6	54.5	40	
Bilateral	174	79.1	64.9	45	
Hepatic resection					0.108
Type of resection					
Limited (< 3 segments)	193	75.7	61.8	43.9	
Major (≥ 3 segments)	98	77.1	58.6	41.4	
Liver curative resection					0.223
Yes	216	77.5	65.3	48.4	
No	21	80.9	60.3	41.3	
Globally curative resection					0.275
Yes	166	76.0	60.1	43.0	
No	71	80.4	68.2	48.8	
Combined treatment modalities to improve resectability					0.089
Yes	23	79.2	58.3	44.6	
No	257	75.8	61.1	43	
Concomitant extrahepatic disease					0.069
Yes	51	73	56.8	38.6	
No	240	76.8	61.6	34.1	
Preoperative chemotherapy					0.119
Yes	192	74.1	60.1	35.9	
No	99	79.7	62.2	38.4	
Clinical response to last line					0.055
Complete response	10	82.4	66.3	52.2	
Partial response	19	80.1	60.1	49.5	
Stabilization	42	47.1	40.4	34.3	
Disease progression	31	33.3	23.4	20.8	
Non-assessable	74	69.4	53.2	48.1	
Total no. of cycles					0.449
≤ 6	96	65.4	50.6	44.4	
> 6	80	72.9	55.7	51.4	
Postoperative chemotherapy					0.217
Yes	154	83.6	64.7	48.6	
No	137	67.9	56.6	47.2	
Abnormal histology of non-tumoral liver parenchyma					
Steatosis	83	77.6	77.1	60.1	0.287
SOS	24	72.4	60.1	53.5	
CHN	5	64.7	52.3	44.5	
CASH	5	68.4	50.6	42.7	
Normal	167	78.9	73.5	66.1	

Chemotherapy-associated steatohepatitis (CASH), Sinusoidal obstruction syndrome (SOS), Coagulative hemorrhagic necrosis (CHN)

Univariate analysis of independent variables was constituted among different age groups to find out if there can be defined any prognostic or influential factors to estimate postoperative survival. Parameters with p values less than 0.1 on univariate analysis were included in multivariate analysis (**Table 4**). Patients who were not treated by globally curative resections had better 1,3, and 5-year survival patterns on both univariate and multivariate analysis (p=0.031).

Table 4. Univariate and multivariate analysis of prognostic factors for survival after recurrence

	No of Patients	3 Year Survival (%)	UV P§	MV P§
Sex			0,112	-
Male	193	59,9		
Female	98	62,7		
Age			0,108	-
<70	185	69,5		
70-75	42	61,7		
75-80	30	64,3		
80<	34	60		
Primary tumour			0,076	NS
Colon	224	60,6		
Rectum	67	61,5		
Liver metastases at diagnosis			0,233	-
No. of metastases				
1–3	241	61,1		
> 3	50	59,5		
Maximum diameter (mm)			0,086	NS
0–50	248	60		
> 50	43	64,9		
Location			0,072	NS
Unilateral	117	54,5		
Bilateral	174	64,9		
Hepatic resection			0,309	-
Type of resection				
Limited (< 3 segments)	193	61,8		
Major (≥ 3 segments)	98	58,6		
Liver curative resection			0,106	-
Yes	216	65,3		
No	21	60,3		
Globally curative resection			0,072	0,031
Yes	166	60,1		
No	71	68,2		
Combined treatment modalities to improve respectability			0,166	-
Yes	23	58,3		
No	257	61,1		
Concomitant extrahepatic disease			0,057	NS
Yes	51	56,8		
No	240	61,6		
Preoperative chemotherapy			0,107	-
Yes	192	60,1		
No	99	62,2		
Clinical response to last line			0,069	NS
Complete response	10	66,3		
Partial response	19	60,1		
Stabilization	42	40,4		
Disease progression	31	23,4		
Non-assessable	74	53,2		
Total no. of cycles			0,336	-
≤ 6	96	50,6		
> 6	80	55,7		
Postoperative chemotherapy			0,405	-
Yes	154	64,7		
No	137	56,6		
Abnormal histology of non-tumoral liver parenchyma			0,224	-
Steatosis	83	71,1		
SOS	24	60,1		
CHN	5	52,3		
CASH	5	50,6		
Normal	169	73,5		

Chemotherapy-associated steatohepatitis (CASH), Sinusoidal obstruction syndrome (SOS), Coagulative hemorrhagic necrosis (CHN)

Assessment of Chemotherapy-induced Liver Lesions and Clinical Outcomes

The dominant histopathological finding was 'steatosis' in 83 patients, 'sinusoidal obstruction syndrome (SOS)' in 24, 'chemotherapy-associated steatohepatitis (CASH)' in 5, and 'coagulative hemorrhagic necrosis (CHN)' in other 5 respectively. Though statistically non-significant, patients with steatotic liver had superiority among others in terms of survival during 1,3, and 5-year follow-ups. Comparison of chemotherapy-induced liver lesions (CILL) associated with postoperative 90-day morbidity rate has not gained a statistical value. CASH was associated with the lowest OS rates (27,4%) (p=0.005), as patients with CHN had better DFS rates among others (p=0.006). The search for a meaningful association between the number of chemotherapy cycles and resultant effects on liver parenchyma in terms of clinical outcomes didn't end with a significant result (p=0.082).

DISCUSSION

We investigated the clinical outcomes of repeat liver resections for both younger (≤70 years) and elderly (70< years) patients and searched for an upper age limit that would provide non-inferior results in terms of survival compared to the younger patients. The present study demonstrated similar rates of 1,3, and 5-year survival for patients aged ≤70, 70-75, 75-80, and 80< years respectively. Advanced age did not lead to an inferior outcome in terms of survival when surgery was performed for selected patients. Multivariate analysis of several independent parameters revealed the globally curative resections as a significant parameter of survival after recurrence.

The outcome of repeat liver resections is diversely appreciated in the literature. A multi-institutional retrospective study including 170 patients from 20 centers has analyzed repeat resections performed for recurrences of CLM of which 32% of long-term survival was reported in selected patient groups with acceptable rates of morbidity and mortality (14). Ziff et al. (15) presented 32 months of median and 32% 5-year survival for patients with extended repeat liver resections in another study. We have demonstrated similar results for the patient groups constituted by ≤70, 70-75, 75-80, and 80< years of age.

The tumor downstaging after neoadjuvant therapy is a good prognostic factor for the long-term outcome (12). We observed favorable 1,3, and 5-year survival outcomes for those who had complete and/or partial response to neoadjuvant therapies compared to those with stable status or having disease progression. In line with current knowledge, response to neoadjuvant therapy played an influential role in survival for the present study as well. Those being non-responsive or acting in a progressive pattern after neoadjuvant therapy had less favorable outcomes for survival on long-term follow-up.

Some of the chemotherapeutics linked with reversible hepatic parenchymal injury, mentioned as CILLs, are accused of elevating the risk of postoperative morbidity and mortality (16). This clinical entity is commonly divided into two groups according to their histopathological features such as chemotherapy-associated fatty liver diseases (Steatosis and CASH) and sinusoidal injuries (CHN, SOS, and nodular regenerative hyperplasia) (17). Controversy exists in current literature regarding the detrimental role of chemotherapy and associated CILLs over clinical outcomes. Such that, T. Pawlik et al. (18) did not find a clinical association between preoperative chemotherapy and postoperative morbidity and mortality. Whereas, Karoui et al. (19) have demonstrated increased morbidity due to preoperative chemotherapy given to CLM patients. Vauthey et al. (20) have demonstrated an elevated risk of 90-day mortality among CLM patients, particularly for those having steatohepatitis due to oxaliplatin chemotherapy compared to those who didn't have steatohepatitis. We didn't observe any significant clinical association between CILLs and pre-defined independent factors (Diabetes mellitus, BMI, intra-operative blood transfusion) and the total number of chemotherapy cycles given. CASH patients had the least favorable postoperative outcomes among other CILLs, and patients with CHN achieved better DFS rates among other CILLs. An interesting finding was the spontaneous disappearance of most CILLs at secondary resections. Those lesions that appear after chemotherapy may mimic metastatic lesions thus it should be kept in mind to prevent unnecessary struggles and possible interventions (21). A few weeks of the non-chemotherapy interval before surgery most likely will ensure the disappearance of these lesions.

Patients who received surgery combined with adjunct therapies like thermal ablation (RFA, MWA), TACE, TARE, or SIRT had taken similar benefits of 1, 3, and 5-year survival compared to those that were only treated by surgery (p=0.089). Those adjuncts may offer clear advantages such as an increased chance of resectability to achieve R0 resection by decreasing tumor burden before the surgery, also tumor ablative therapies may allow less radical and safe surgeries to be performed (22). Current literature favors surgery over other treatment methods for providing the best survival outcomes (23-25). Alternative therapies should be reserved for unresectable cases that are not eligible for surgery, for palliative purposes, or as a bridging therapy to decrease tumor burden that may have a chance of resection later on in the future.

No clear benefit in terms of survival was stated between unilobar or bilobar involvement of CLM. As in both circumstances, comparable long-term outcomes can be achieved (26,27). In a multicentric ALLPS cohort study published by Petrowsky et al. (28) which included 510 CLM patients from 22 different centers; the size of metastasis and site of involvement (Unilobar vs bilobar) were not found as predictive factors of cancer-specific survival. We achieved close rates of 1, 3, and 5-year survival for patients with unilobar and bilobar involvements consecutively (p=0.058). We may attribute this to successfully performed R0 resections for the majority of the patients independent of unilobar or bilobar involvement. Likewise, we did not observe a significant difference among survival rates for those with different tumor diameters. Complete tumor removal with respect to R0 resection is crucial for optimum survival.

In a similar study from our center, unresectable CLM patients that were given chemotherapy before surgery were compared with upfront resected ones. Even though 38% of the patients that were resected had previously known extra-hepatic site involvements, this demonstrated no clinical impact on survival outcomes (29). Likewise, the presence of concomitant extra-hepatic metastasis didn't have a significant role in the survival rate according to multivariate analysis in our cohort as well.

There was no significant difference in terms of survival between non-anatomic and anatomic liver resections of 288 consecutive patients with CLM recurrences which was previously reported by our team (30). Non-anatomic liver resections offer shorter operative times and less requirement of blood transfusion by leaving more remnant liver volume behind which enables a lower risk of postoperative liver failure compared to anatomic resections as both types of resections provide similar oncological benefits for repeat liver resections of CLM recurrences (31,32). Our findings support performing non-anatomic resections with respect to non-inferior outcomes in all patient groups compared to anatomic resections.

CONCLUSION

This is the first documentation of long-term outcomes of resections performed for liver recurrences of CLMs among both younger and elderly patients. Elderly patients have gained similar 1,3, and 5-year survival rates compared to younger patients following repeat resections. Upper age solely shouldn't be a contradiction in the case of redo surgery as well when well-selected patients are offered for resection. Chemotherapy should be considered at the perioperative setting as the clinical association of CILLs with long-term outcomes should be elucidated with future prospective studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Istanbul Göztepe Prof. Dr. Süleyman Yalçın City Hospital Clinical Researches Ethics Committee (Date: 22.02.2023, Decision No: 2023/0124).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflicts of interests: The author certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Author Contribution: The author declare that he has participated in the design, execution, and analysis of the paper and he has approved the final version.

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