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Major Hepatectomy for Colorectal Metastases in the Elderly: A Tertiary Center Experience

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The purpose of this retrospective study was to investigate whether patients over 70 years old are at significantly higher risk for worse outcomes following major liver resection. Hepatic resection is the only treatment offering long-term survival for patients with colorectal liver metastases. As the population considered for metastasectomy is aging, there are still controversial published results regarding the safety of major hepatectomy in elderly patients. Between December 2002 and April 2010, 327 patients underwent major liver resection for colorectal liver metastasis. Patients were stratified into 2 groups: group A, <70 years old; and group B, ≥70 years old. Recorded, analyzed, and compared data across groups included the following: (1) patient characteristics including age, sex, American Society of Anesthesiologists performance status, primary tumor site and stage, adjuvant chemotherapy, number and size of metastatic lesions; (2) perioperative data including extent of resection, in-hospital mortality, postoperative morbidity, length of hospital stay, length of intensive treatment unit stay and blood loss; and (3) overall survival. The patients' characteristics were similar as were the characteristics of their tumors. There was no difference in overall morbidity (25% versus 22%) or postoperative mortality (2.6% versus 2.9%) ($P = 0.44$ and 0.57, respectively). The overall survival was 67% versus 62% in group A and B, respectively ($P = 0.09$). Elderly patients can safely undergo major liver resection for colorectal liver metastases with short- and long-term outcomes comparable with younger patients.

Key words: Hepatectomy – Major liver resection – Colorectal cancer liver metastasis – Elderly – Overall survival

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Colorectal cancer is the third most common cancer in the United Kingdom following breast and lung primaries. Its occurrence is strongly correlated with age, with 86% of cases arising in people who are 60 years old or older.[1] Since general population life expectancy is rising rapidly thanks to improved health care services, providing care to the elderly population has become an increasingly important component of the surgeon's workload.

About 10% to 25% of patients with colorectal cancer have liver metastases at the time of primary diagnosis, and another 20% to 25% develop metachronous liver metastases.[2–4] Hepatic resection has been the only treatment that can offer long-term survival for patients with colorectal liver metastases (CLM), with acceptable mortality and morbidity rates.[5–7] The safety of minor liver resections, defined as resections involving 3 or less Couinaud segments, for CLM in the elderly has been well established,[7] but several studies are still examining the outcome of major liver resection in these patients, with some suggesting that age does not appear to be a risk factor influencing short- and long-term outcomes,[8–10] while others suggest that doubt still remains regarding the benefits of hepatic resection in the elderly because patients older than 70 years constitute only 8% to 15% of the pool of patients undergoing liver resection for CLM.[7,11,12]

The aim of this study was to evaluate the short- and long-term outcomes following major hepatic resection for CLM in patients 70 years of age and older.

Materials and Methods

Between December 2002 and April 2010, 327 patients underwent major liver resection for CLM. Patients were divided into 2 groups: group A, <70 years old; and group B, ≥70 years old. Patients' records were reviewed and analyzed retrospectively. Patient characteristics, perioperative course, and survival were compared across the 2 groups. Preoperative diagnosis of CLM was made based on radiologic features. A contrast-enhanced computed tomography (CT) scan of the chest, abdomen, and pelvis was obtained to assess local and distant extent of the tumor, and a magnetic resonance imaging (MRI) scan of the liver was obtained in cases of undetermined lesions, for further characterization. Positron emission tomography (PET)/CT scans were obtained in cases of clinical and radiologic suspicion of extrahepatic metastases.

Major liver resection was defined as resection of 4 or more Couinaud liver segments. Liver resection was attempted provided that resection was potentially curative with sufficient predicted remnant liver.

All patients were reviewed in a preadmission clinic by an anesthesiologist. Symptom-limited stair-climbing test was performed on all patients. Comorbidities were investigated with complete blood tests, chest X-ray, electrocardiogram, respiratory function test, and blood gas analysis. Echocardiography and exercise tolerance electrocardiogram were carried out only in patients with a medical history of coronary artery disease. A cardiologist and pulmonologist were involved in the preoperative evaluation of patients with uncontrolled or high-grade heart or lung disease, respectively.

Operative mortality was defined as death within 90 days from the operation. Perioperative complications were defined as any adverse event occurring between the induction of anesthesia and the 30th day after the operation that required deviation from standard postoperative management. Transient liver failure was defined as a prolonged prothrombin time >18 seconds or serum bilirubin concentration >30 μmol/L.

Following discharge, patients were monitored regularly for tumor recurrence by clinical history, physical examination, CT scans of the chest, abdomen, and pelvis, and tumor markers. Follow-up was carried out every 3 months in the first year after the operation, then every 6 months for the following 2 years. Thus, a 3-year follow-up was considered complete for all included patients.

Statistical analysis of collected data was conducted using SPSS software Version 20 (IBM Corp, Chicago, Illinois); χ^2 test and Mann-Whitney *U* tests were used for unifactorial analyses; and Kaplan-Meier analysis was additionally applied for survival analysis. A *P* value of <0.05 was considered statistically significant.

Results

Characteristics of both patients and tumors are shown in Table 1. Rectal primary was more frequent in the younger group, but there was no difference in Duke's staging. The total tumor size was significantly larger in group B, but there was no difference in the tumor number.

Postoperative outcomes are summarized in Table 2. There was no difference in postoperative mortality, and the rate of perioperative complications was

Table 1 Patient and tumor characteristics (numbers in brackets are percentages unless otherwise specified)

	<70 years	≥70 years	*P* value
No. of patients	189	138	
Age, mean ± SD	59.7 ± 7.5	75.6 ± 3.9	0.002
Sex, n (%)			0.92
Male	113 (60)	85 (61)	
Female	76 (60)	53 (39)	
ASA, n (%)			
1	80 (42)	44 (32)	
2	43 (23)	40 (29)	0.095
3	66 (35)	54 (39)	
Primary tumor, n (%)			
Rectal, n (%)	84 (44)	46 (33)	0.031
Colon, n (%)	105 (56)	92 (67)	
Duke's stage, n (%)			
A	3 (2)	0	
B	73 (39)	51 (37)	0.45
C	113 (59)	87 (63)	
Adjuvant chemotherapy, n (%)	158 (84)	102 (74)	0.23
Synchronous/ metachronous metastases	74/115	48/90	<0.01
Solitary/multiple metastases	70/119	53/85	0.63
No. of tumors (mean ± SD)	2.6 ± 1.8	2.7 ± 1.7	0.9
Size of tumor (mean ± SD)	29 ± 20	33.6 ± 26	<0.01
PVE, n (%)	13 (7)	8 (6)	0.89
Radicality of resection			
R0, n (%)	183 (97)	130 (94)	0.7
R1, n (%)	6 (3)	8 (6)	
Type of resection, n (%)			
Right hepatectomy	107 (57)	84 (61)	
Extended right hepatectomy	43 (23)	22 (16)	0.1
Left hepatectomy	25 (13)	28 (20)	
Extended left hepatectomy	14 (7)	4 (3)	

PVE, portal vein embolization.

Table 2 Early postoperative outcome (numbers in brackets depict range of observations)

	<70 years	≥70 years	*P* value
Mortality, n (%)	5 (2.6%)	4 (2.9%)	0.57
Morbidity, n (%)	48 (25%)	30 (22%)	0.44
Hospital stay, d (mean ± SD)	17 ± 10	17.5 ± 11	0.7
ITU stay, d (mean ± SD)	6 ± 7	6.3 ± 7	0.8
Blood loss, number of units of packed red blood cells (mean ± SD)	2.7 ± 3	2.2 ± 2	0.059

also similar. In group A, the overall incidence of postoperative complications was 25%; the most common complication was transient liver failure, and all resolved within the first 3 postoperative weeks. Eleven patients had pneumonia managed by antibiotics +/− ventilatory support, while in 4 of these, infection progressed to multi-organ failure, and they died. Twelve patients had bile leakage, which was managed with drainage +/− endoscopic retrograde cholangiography, sphincterotomy, and stenting. Intra-abdominal hemorrhage complicated 1 case, and the patient was re-operated on the third postoperative day for control of bleeding. One patient developed bowel ischemia on the third postoperative day and was subsequently subjected to extended right hemicolectomy but eventually progressed to multi-organ failure and died on the 10th postoperative day. In group B, the overall incidence of postoperative complications was 22%; the most common complication was pneumonia, which progressed to multi-organ failure in 4 patients, who eventually died while still in the hospital. One patient from group B had a myocardial infarction on the second postoperative day and was managed in a cardiac care unit for 4 days (Table 3). The mean hospital stay, intensive treatment unit (ITU) stay, and blood transfusion were similar between the 2 groups.

The overall average follow-up period for both groups was 40.2 ± 25 months (range, 1–103 months). Twenty-five patients (13%) from group A had a second hepatic resection as a treatment for recurrence in comparison with 19 patients (14%) from group B ($P = 0.96$), and all repeat resections for CLM recurrence were minor resections (3 or less segments). Overall survival rates after hepatic resection did not differ significantly between the 2 groups (Fig. 1). The mean overall survival for group A was 66 ± 3.1 years (limited to 103 years) versus 64 ± 3.7 years (limited to 99 years) for group B ($P = 0.98$). The 1- and 3-year survival rates in group A and B were 89% versus 82% ($P = 0.6$) and 67% versus 62% ($P = 0.09$), respectively.

Table 3 Postoperative complications

Complication, n (%)	<70 years	≥70 years	*P* value
Pneumonia	11 (6)	14 (10)	>0.1
Bile leak	12 (6)	5 (4)	>0.1
Transient liver failure	14 (8)	2 (2)	>0.1
Bleeding	1 (0.5)	0	>0.1
Abscess	6 (3)	7 (5)	>0.1
Wound infection	3 (2)	1 (1)	>0.1
Myocardial infarction	0	1 (1)	>0.1
Bowel ischemia	1 (0.5)	0	>0.1

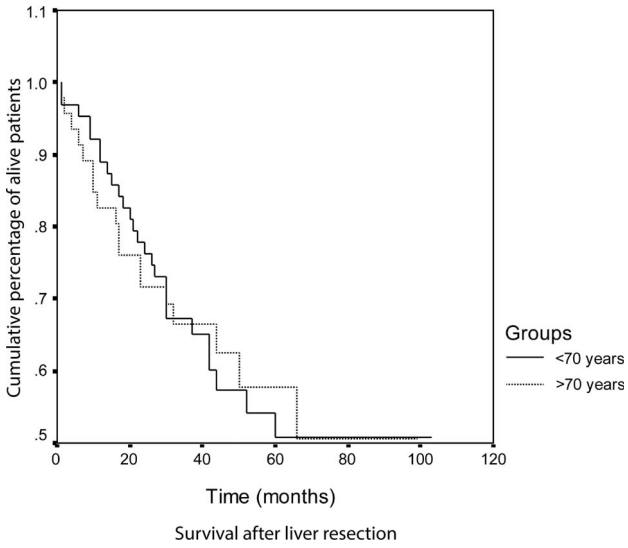

Fig. 1 Kaplan-Meier curves for overall survival in each age group (Log rank; $P = 0.988$).

Discussion

Over the last few years, there has been an ongoing debate regarding whether major liver resection can be performed in the elderly with similar safety profiles to younger patients, or if it is an unreasonable approach that carries poorer outcomes. Since the beginning of this debate, there have been many studies supporting major liver resection in the elderly, reporting acceptable morbidity and mortality rates.[8–10,12–16] Yet, some reports have linked increased age to increased mortality rates following hepatectomy for CLM.[8,13,17] Besides this debate, the daily clinical practice has been characterized by a relative reluctance to offer elderly patients similar treatment options as are offered to their younger counterparts. That is evident because patients aged 75 years or older are less likely to undergo resection of colorectal cancer liver metastases compared with younger patients.[18,19] Furthermore, recent prospective randomized controlled trials on colorectal cancer liver metastases and hepatocellular carcinoma (HCC) have included few elderly patients relative to the high proportion of elderly among disease cohorts.[20] Moreover, it has been reported that the elderly are less likely to be treated with chemotherapy either alone or in the adjuvant setting compared with younger counterparts for all cancers and especially for colorectal cancer.[21–23]

The present study suggests encouraging results in elderly patients treated with major liver resection for CLM. Forty-two percent of patients in this cohort were 70 years old or older, which is the arbitrary age cutoff used in most reports, reflecting the aggressive approach adopted in treating these patients, justified by very encouraging studies concluding on the safety of major liver resection in the elderly.[13,14] The authors report a perioperative mortality rate of 3%, perioperative morbidity of 22%, and a 3-year survival of 62%. Reported perioperative mortality corresponds to the lowest reported rates in the literature, with a recent meta-analysis concluding on a 3.6% median rate,[24] despite the use of a lower cutoff of 65 years in some cases.[13] Similarly, the aforementioned 3-year survival is slightly above the reported range 38% to 57%.[9,13] Reported morbidity seems notably lower compared with rates of 27% to 32.3% suggested in the literature.[9,13] However, although in most cases, including the aforementioned meta-analysis, morbidity between age groups is statistically significant, this was not confirmed in the present study.

This is one of the few studies that demonstrate equivalent outcomes between elderly and younger patients. It has to be mentioned though that in the present series, there was no statistical difference in American Society of Anesthesiologists (ASA) score to start with, which is not very frequent in the literature, and it can be argued that this difference in performance status may be the strongest contributing factor to worse outcomes. It should also be underlined that outcomes reported in the present study come from a tertiary large-volume center and from a highly skilled and experienced team, thus conclusions cannot be easily generalized. Finally, several factors that can influence outcomes and have been studied in the literature as potential confounding factors have not been included in a multifactorial analysis in the present study, either because they were not statistically significantly different between groups (such as blood loss, operation duration, and performance status) or because a standardized approach was followed in all cases (nutritional support, standardized open hepatectomy, and postoperative monitoring of liver function).

In conclusion, it seems reasonable to argue that elderly patients can safely undergo major liver resection for CLM, with short- and long-term outcomes comparable with younger patients. Therefore, eligibility for major liver resection should not rely on chronologic age alone but rather be a decision of a well-structured multidisciplinary team that can encompass all contributing factors.

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