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Age Greater than 60 Years in Patients Undergoing Liver Resection for Colorectal Liver Metastases is an Independent Prognostic Factor of an Increased Postoperative Non-Surgical Complication Rate and of Overall Survival

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Abstract

Aim: To evaluate the effect of advanced age on peri-operative complications, recovery of liver function and overall survival in patients undergoing hepatectomy for colorectal liver metastases.

Methods: Consecutive patients with colorectal liver metastases, who underwent potentially curative hepatectomy in two institutions in the UK from 2005 to 2012, were enrolled in this retrospective study. For each patient the institutional electronic records were interrogated and data were collected.

Results: A total of 260 patients were enrolled, 150/260 (57.7%) of whom were older than 60 years of age. 113 complications were recorded occurring in 97/260 of patients (37.3%). Univariate analysis of factors influencing the peri-operative morbidity showed that there was a significant association with an age greater than 60 years. This association remained significant in multivariate analysis (HR 1.92; 95% CI, 1.10-3.36; P=0.02). The number of technical surgical complications was comparable between the young and older group of patients (p=0.449). However, complications, which were not surgical such as pulmonary and cardiovascular, were higher in the older age group (p=0.031). Indices of pre-operative liver function (bilirubin, albumin, ALT) were comparable between the two age groups (p>0.5) and there was no difference in functional recovery of the liver. Although age greater than 60 years was not associated with reduced DFS, it was associated with decreased OS both in univariate and multivariate analysis (HR 2.45; 95% CI, 1.41-4.25 ;P=0.001).

Conclusion: An age greater than 60 years is an independent prognostic factor of an increased postoperative non-surgical complication rate and of decreased overall survival in patients undergoing partial hepatectomy for colorectal liver metastases. In this age group of patients significant post-operative complications relate not to the technical complexities or scale of procedure, but to the baseline physiological performance characteristics of the patient.

Key words: *Hepatectomy; elderly; survival; complications*

Introduction

A recent editorial in Lancet highlighted the importance of care of older people, as they face specific health problems related to their age, with stroke and ischaemic heart disease being among the biggest causes of years of life lost in the population group older than 60 years of age [1]. There are reports, which have shown no differences between elderly and younger patients with regard to morbidity and mortal-

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ity following an operation [2,3,4]. Rising life expectancy worldwide in the last century has led to elderly patients being surgically managed more frequently [5-7]. Despite the overall improvements in surgical outcome, the additional risks linked with surgery in the elderly patients have not been investigated fully [8-11].

Partial hepatectomy is a commonplace as part of treatment for metastases from colon and increasingly other malignancies [9]. Early surgical outcomes depend greatly on the extent of the operation and the host liver function [12]. Morbidity rates are reported as 30%, although mortality rates are very small [13-16]. Reports so far are conflicting in regard to comorbidity, compromise of hepatic, renal and cardiopulmonary function with several indicating both higher postoperative mortality and morbidity rates related to age [17,18], and others not being able to show any difference after liver resection and in relation to aging in a setting of CRLM [19].

The aim of this study is to assess the safety and long-term results of partial hepatectomy of colorectal metastases in elderly patients by comparison with a younger cohort. We have excluded patients undergoing hepatectomy for HCC, due to the heterogeneity of this population and we focused on patients with CRLM. For the same reason we excluded patients with NET. We decided to use the age of 60 years as a threshold, since people older than that begin to be prone to coronary heart disease and development of other co-morbidities [11] and it also approximates to the age of retirement in the UK which is around 63.8 years of age.

Materials and methods

Electronic records of patients who underwent hepatectomy at the Royal Marsden Hospital and at The London Clinic for CRLM from January 2005 to December 2012 were examined in the prospectively maintained surgical database: Demographic characteristics (sex, age at diagnosis of primary tumour and metastatic disease as well as extent of partial hepatectomy). With regard to CRLM, data were collected concerning the number and distribution of metastases at the time of diagnosis, as well as at the time elapsed between diagnosis of primary tumour and that of liver metastases. Metastatic disease within 1 year after the diagnosis of the primary tumour was defined as synchronous CRLM and those diagnosed beyond 1 year were defined as metachronous. Additionally, the type of preoperative chemotherapy received and the number of cycles of chemotherapy administered were recorded, as well as the type of hepatectomy, the postoperative complications and their management and the length of stay in hospital. Disease free survival and overall survival, liver functional parameters including serum total bilirubin, albumin level, and serum levels of alanine aminotransferase (ALT) were also recorded.

All patients underwent pre-operative assessment by computed tomography (CT) of the chest, abdomen, and pelvis and, in most cases, Fluorodeoxyglucose-positron emission tomography (FDG-PET), to exclude extrahepatic metastases and magnetic resonance imaging (MRI) to determine the extent of liver disease. FDG-PET was commenced as part of the standard pre-operative assessment and staging after 2008. Tumour response to chemotherapy was assessed with magnetic resonance imaging and Response Evaluation Criteria in Solid Tumors. Resectability was evaluated based on a multidisciplinary review. Progression of disease under chemotherapy or presence of extrahepatic disease was considered relative but not an absolute contraindication to hepatectomy. All patients were discussed at the multidisciplinary meeting (MDM).

Liver Resection

Intra-operative ultrasound was used with an aim to detect occult tumours and plan the most appropriate resections. Portal vein embolization was performed 4 weeks before surgery, when an extended hepatectomy was planned, if the future liver remnant was considered to be inadequate (with ratios <30% for liver remnant to whole liver volume).

Major hepatectomy was defined as resection of three or more liver segments, with liver resections being classified as anatomical or non-anatomical, depending on the segmental anatomy of the liver. Resections were categorised, being either complete with negative microscopic margins (R0), or incomplete with microscopically (R1) or macroscopically (R2) positive margins. In patients where the primary tumour was in situ, the decision was made by the multidisciplinary team whether to proceed to a synchronous resection of the primary tumour and CRLM or a 'liver first' approach, taking into account the general health of the patient and the extent of necessary hepatectomy [20].

Complications

Postoperative complications were graded on a 1-to-5 scale according to the *Clavien-Dindo* Classification of Surgical *Complications [21].* Grade I and II complications were considered as minor complications, grade III and IV as major, and grade V as the postoperative deaths. Perioperative mortality was defined as deaths occurring during the operation or in the same hospital admission in regards or within 30 days from the operation.

Statistical Analysis

Statistical analyses were performed with the Statistical

Package of the Social Sciences (SPSS), version 17.0. The primary end points of the study were perioperative morbidity and OS. The patients were grouped according to their age at the time of hepatectomy, as younger than 60 years and as older than 60 years. Chi-square test (for categorical variables) and Mann-Whitney U test (for continuous variables) were used for calculating the association between patients' and tumour's characteristics and age. Univariate and multivariate analyses of perioperative morbidity were performed by using logistic regression models.

OS was calculated from the time of diagnoses of liver metastasis to the date of cancer-related death and was censored at the last follow up or at the time of unrelated to cancer death. The impact of categorical variables on OS was analysed using the Kaplan-Meier method. Survival outcomes between groups were compared with the log-rank test. A P value of less than 0.05 was considered statistically significant. The factors which were found to be associated with the OS (P>0.1) in univariate analysis were used for the multivariate Cox-regression analysis.

Results

A total of 260 patients, who had undergone partial hepatectomy for CRLM, were enrolled. 100 patients that had undergone liver resection for non- colorectal liver metastases were excluded. The demographic characteristics of the patients, the characteristics of CRLM, preoperative systemic chemotherapy and the characteristics of liver resection are shown in Table 1. 110 patients (42.3%) were aged <60 years, and the remaining 150 patients (57.7%) were >60 years. The two groups (<60 vs>60 years) were comparable regarding the severity of the disease (number of liver metastases and their distribution, size of biggest liver metastasis, presence of extrahepatic disease, interval between diagnosis of primary tumour and that of metastasis) (Table 1). However, there

Table 1. *Demographics, Tumour, and treatment Characteristics*

Variable	Age ≤ 60 N=110(42.3)	Age >60 N=150(57.7)	Total N=260	*P* Value
Patient' characteristics Gender				
Male	56(49.1)	105(70)	161(61.9)	
Female	54(49.1)	45(30)	99(38.1)	**0.002**
CRLM characteristics Timing of metastasis				
Synchronous	81(73.6)	99(66)	180(69.2)	
Metachronous	29(26.4)	51(34)	80(30.8)	0.187
No. of liver metastases Mean ± SD	3.2±3.3	2.8±2.5	3±2.8	0.468
No. of metastasis at diagnosis				
≤ 3	79(71.8)	109(72.7)	188(72.3)	
>3	31(28.2)	41(27.3)	72(27.7)	0.880
Distribution of Lesions				
Unilobar	64(58.2)	97(64.7)	161(61.9)	
Bilobar	46(41.8)	53(35.3)	99(38.1)	0.287
Size of Bigger Lesion Mean ± SD, mm	39.2 ±30.4	34.4±24.1	36.3±26.9	0.514
Size of largest metastases				
≤ 5cm	82(74.5)	125(83.3)	207(79.6)	
>5cm	28(25.5)	25(16.7)	53(20.4)	0.082
Extrahepatic Disease				
No	98(89.1)	131(87.3)	229(88.1)	
Yes	12(10.9)	19(12.7)	31(11.9)	0.666
Preoperative Chemotherapy Preoperative Chemotherapy				
Yes	101(91.8)	135(90)	236(90.8)	
No	9(8.2)	15(10)	24(9.2)	0.617

Table 1. *Demographics, Tumour, and treatment Characteristics (continued).*

Variable	Age ≤ 60 N=110(42.3)	Age >60 N=150(57.7)	Total N=260	*P* Value
Preoperative Biologic Agents (Bevacizumab or Cetuximab)*				
Yes	60(59.4)	62(45.9)	122(51.7)	
No	37(36.6)	70(51.9)	107(45.3)	0.026
Unknown	4(4)	3(2.2)	7(3)	
Oxaliplatin vs Irrinotecan*				
Oxaliplatin-based chemotherapy	61(60.4)	95(70.4)	156(66.1)	
Irinotecan- based chemotherapy	33(32.7)	37(27.4)	70(29.7)	0.257
Other or Unknown Regimen	7(6.9)	3(2.2)	10(4.2)	
Total No of Chemotherapy Cycles Mean ± SD*	7.3±4	6.6±3.5	6.9±3.7	0.151
Number of Neoadjuvant Chemotherapy Cycles*				
<4	27(26.7)	50(37%)	77(32.6)	
>4	61(60.4)	78(57.8)	139(58.9)	0.206
Unknown	13(12.9)	7(5.2)	20(8.5)	
Response to neoadjuvant chemotherapy*				
Responders[+]	91(90.1)	122(90.4)	213(90.3)	
Progression	10(9.9)	13(9.6)	23(9.7)	0.945
Liver Resection				
Type of liver resection				
Major	69(62.7)	75(50)	144(55.4)	
Minor	41(37.3)	75(50)	116(44.6)	**0.041**
Synchronous Resection of primary tumour				
No	86(78.2)	132(88)	218(83.8)	
Yes	24(21.8)	18(12)	42(16.2)	**0.034**
Portal Vein Embolization				
No	101(91.8)	136(90.7)	237(91.2)	
Yes	9(8.2)	14(9.3)	23(8.8)	0.747
RFA in addition to resection(pre-, intra-, postoperatively)				
No	90(81.8)	133(88.7)	223(85.8)	
Yes	20(18.2)	17(11.3)	37(14.2)	0.118
Perioperative Morbidity				
No	77(70)	86(57.3)	163(62.7)	
Yes	33(30)	64(42.7)	97(37.3)	**0.037**
Perioperative Mortality				
No	109(99.1)	148(98.7)	257(98.8)	
Yes	1(0.9)	2(1.3)	3(1.2)	0.999

**only for patients received neoadjuvant chemotherapy*

[+]Radiologic Complete Response or Radiologic Partial Response or Stable Disease (according to RECIST)

Synchronous: diagnoses of CRLM within 12 months from the diagnosis of primary tumour

**Pearson Chi-Square Test*

***Mann-Whitney U Test*

[++]"Liver First Approach" or " synchronous resection"

were differences between the two groups with regard to the systemic preoperative chemotherapy. Patients older than 60 years received biological agents such as bevacizumab and cetuximab (p=0.026) less frequently.

Complications

From the total of 260 patients, 97 patients (37.3%) experienced 113 complications. The overall complication rate is presented in Table 1 and their management is presented in Supplementary Table 1. Forty-seven patients (18.1%) experienced major complications.

Univariate analysis of factors influencing the perioperative morbidity (Table 2) showed that age greater than 60 years (p=0.037), the number of liver metastases (more than 3) (p=0.004), pre-operative administration of more than 4 cycles of systemic chemotherapy (p=0.012), and major liver resection (p=0.004) were significantly associated. When age was analyzed as a continuous variable, there was a trend of association, which did not reach levels of statistical significance (p=0.095). Multivariate analyses adjusted to age, sex, number of liver metastases, type of neoadjuvant cytotoxic chemotherapy, number of cycles of neoadjuvant chemotherapy, and the extent of hepatectomy, revealed that an age greater than 60 years (HR 1.92; 95% CI, 1.10-3.36; P=0.02) and major hepatectomy (HR 1.89; 95% CI, 1.05-

Table 2. *Univariate analysis for perioperative morbidity and overall survival.*

		Morbidity			OS	
Parameter	N(%)	NO(163)	YES(97)	P-value	HR(95% CI)	*P*-value
Patient' characteristics						
Gender						
Female	99(38.1)	69(42.3)	30(30.9)	0.067	1(referent)	
Male	161(61.9)	94(57.7)	67(69.1)		1.17(0.72-1.91)	0.510
Age						
≤ 60	110(42.3)	77(47.2)	33(34)		1(referent)	
>60	150(57.7)	86(52.8)	64(66)	0.037	2.14(1.28-3.58)	**0.004**
CRLM characteristics Timing of metastasis						
Synchronous	180(69.2)	108(66.3)	72(74.2)		1(referent)	
Metachronous	80(30.8)	55(33.7)	25(25.8)	0.178	1.15(0.72-1.84)	0.546
No. of metastasis at diagnosis						
≤ 3	188(72.3)	128(78.5)	60		1(referent)	
>3	72(27.7)	35(21.5)	37	**0.004**	1.29(0.76-2.21)	0.340
Distribution of Lesions						
Unilobar	161(61.9)	106(65)	55(56.7)		1(referent)	
Bilobar	99(38.1)	57(35)	42(43.3)	0.181	1.37(0.85-2.21)	0.185
Size of largest metastases						
≤ 5cm	207(79.6)	131(80.4)	76		1(referent)	
>5cm	53(20.4)	32(19.6)	21	0.696	1.31(0.76-2.24)	0.327
Extrahepatic Disease						
No	229(88.1)	143(87.7)	86(88.7)		1(referent)	
Yes	31(11.9)	20(12.3)	11(11.3)	0.823	1.38(0.59-3.20)	0.453
Preoperative Chemotherapy						
Preoperative Chemotherapy						
No	24(9.2)	15(9.2)	9(9.3)		1(referent)	
Yes	236(90.8)	148(90.8)	88(90.7)	0.984	0.94(0.43-2.06)	0.887

Table 2. *Univariate analysis for perioperative morbidity and overall survival (continued).*

		Morbidity			OS	
Parameter	N(%)	NO(163)	YES(97)	P-value	HR(95% CI)	*P*-value
Preoperative Biologic Agents (Bevacizumab or Cetuximab)*						
No	107(45.3)	69(46.6)	38(43.2)		1(referent)	
Yes	122(51.7)	74(50)	48(54.5)	0.550	0.96(0.60-1.56)	0.899
Unknown	7(3)	5(3.4)	2(2.3)			
Oxaliplatin vs Irinotecan*						
Oxaliplatin-based chemotherapy	156(66.1)	104(70.3)	52(59.1)		1(referent)	
Irinotecan- based chemotherapy	70(29.7)	38(25.7)	32(36.4)	0.075	1.22(0.74-2.03)	0.429
Other or Unknown Regimen	10(4.2)	6(4.1)	4(4.5)			
Number of Neoadjuvant Chemotherapy Cycles*						
<4	77(32.6)	57(38.5)	20(22.7)		1(referent)	
>4	139(58.9)	79(53.4)	60(68.2)	**0.012**	0.86(0.53-1.39)	0.551
Unknown	20(8.5)	12(8.1)	8(9.1)			
Response to neoadjuvant chemotherapy*						
Responders^{+}	213(90.3)	133(89.9)	80(90.9)		1(referent)	
Progression	23(9.7)	15(10.1)	8(9.1)	0.794	2.44(1.30-4.58)	**0.005**
Liver Resection						
Type of liver resection						
Minor	116(44.6)	84(51.5)	32(33)		1(referent)	
Major	144(55.4)	79(48.5)	65(67)	**0.004**	1.33(0.84-2.11)	0.212
Synchronous Resection of primary tumour						
No	218(83.8)	139(85.3)	79(81.4)		1(referent)	
Yes	42(16.2)	24(14.7)	18(18.6)	0.417	0.70(0.32-1.53)	0.381
Portal Vein Embolization						
No	237(91.2)	150(92)	87(89.7)		1(referent)	
Yes	23(8.8)	13(8)	10(10.3)	0.522	1.58(0.72-3.46)	0.253
RFA in addition to resection(pre-, intra-, postoperatively)						
No	223(85.8)	141(86.5)	82(84.5)		1(referent)	
Yes	37(14.2)	22(13.5)	15(15.5)	0.661	2.32(1.30-4.12)	**0.004**

3.40 ;P=0.034) were the only factors independently related to influencing the perioperative morbidity (Table 3). The frequency of major complications was comparable between young and old group of patients (p=0.671).

Although the frequency of surgical complications was comparable between young and old patients (p=0.449), the rate of non-surgical complications (pulmonary, cardiovascular) was higher in the older patient group (p=0.031) (Table 4). Pre-operative serum liver function parameters (bilirubin, albumin, ALT) were comparable between the two age groups (p>0.5) and there was no difference in functional recovery of liver function (Figure 2).

There was no difference in mortality between the two groups with three deaths during the hospital stay. One from liver insufficiency in a young patient and two from the group of old patients; one death due to pneumonia and the other as result of an infected intrabdominal collection with an overall mortality risk of 3/260 (1%).

End Point of Overall Survival

The median follow-up period was 31 months (1 to 107

Table 3. *Multivariate analysis of factors affecting perioperative morbidity and overall survival.*

	Morbidity		OS	
Parameter	HR(95% CI)	*P*-value	HR(95% CI)	*P*-value
Male Gender	1.48(0.84-2.59)	0.169		
>3 metastasis at diagnosis	1.73(0.93-3.24)	0.083		
Irinotecan-based chemotherapy	1.05(0.65-1.72)	0.820		
>4 cycles of neoadjuvant	1.36(0.80-2.32)	0.254		
Major liver resection	1.89(1.05-3.40)	**0.034**		
Age at operation >60 years	1.92(1.10-3.36)	**0.022**	2.45(1.41-4.25)	**0.001**
Disease progression during neoadjuvant chemotherapy			2.24(1.17-4.31)	**0.015**
Perioperative RFA			2.22(1.21-4.05)	**0.010**

Table 4.

	Number of Patients		
Variable	<60 N=110	>60 N=150	*P* Value
Overall complications	33	64	0.037
Major Complications	15	32	0.671
	Number of complications		
Variable	<60 N=39	>60 N=74	*P* Value
Surgical Complications	29	46	0.449
No surgical Complications	10	28	0.031

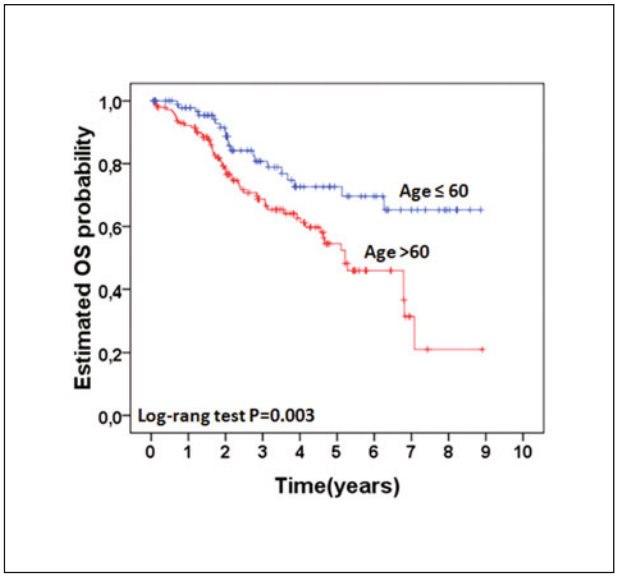

Figure 1. Age and Overall Survival.

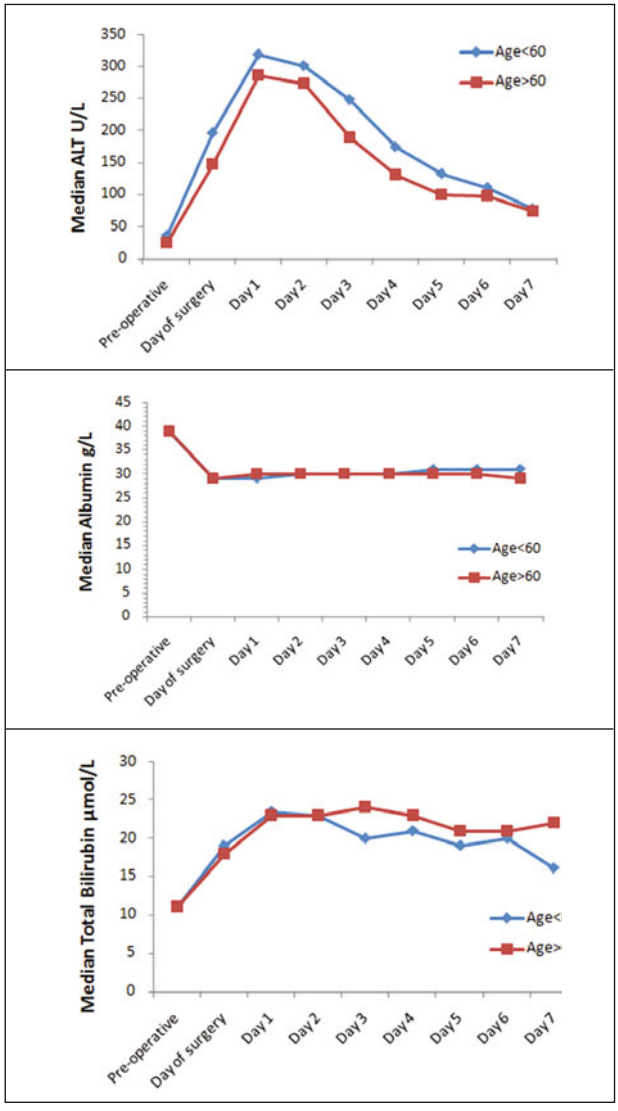

Figure 2. The effect of Age on pre- and postoperative liver function tests.

months). For the entire study population one, three and five-year OS rates were 94%, 73% and 61% respectively.

The results of univariate analyses failed to demonstrate an association between age greater than 60 and DFS (HR 1.02; 95% CI, 0.73-1.41 ;P=0.889). Clinicopathologic factors associated with a decreased DFS were the number of liver metastases at diagnosis (more than 3) (HR 1.99; 95% CI, 1.37-2.89 ;P<0.001), bilobar distribution of lesions (HR 1.88; 95% CI, 1.34-2.63 ;P<0.001), disease progression during neoadjuvant chemotherapy according to RECIST criteria (HR 2.05; 95% CI, 1.26-3.34 ;P=0.004), pre-operative portal vein embolization (HR 2.18; 95% CI, 1.27-3.74 ;P=0.005), and major liver resection (HR 1.45; 95% CI, 1.05-2.00 ;P=0.023). In the multivariate analysis bilobar distribution of lesions (HR 1.56; 95% CI, 1.05-2.32 ;P=0.025) and disease progression during neoadjuvant chemotherapy (HR 2.25; 95% CI, 1.36-3.71 ;P=0.001) remained significant for DFS.

Regarding OS, the results of univariate analyses revealed that age greater than 60 years (HR 2.14; 95% CI, 1.28-3.58; P=0.004), disease progression during neoadjuvant chemotherapy according to RECIST criteria (HR 2.44; 95% CI, 1.30-4.58 ;P=0.005) and pre-, intra- or post-operatively RFA in addition to liver resection (HR 2.32; 95% CI, 1.30-4.12 ;P<0.001) were associated with decreased OS (Table 2). Old patients showed a median OS of 63 months. (Figure 1) with three and five-years rates of 69% and 54% respectively, compared to 81% and 72% respectively in the young patient group. For OS the multivariate analysis was adjusted for age at hepatectomy, response to neoadjuvant chemotherapy and peri-operative RFA.

In the multivariate analysis, all three variables associated with OS in the univariate analysis [age greater than 60 years (HR 2.45; 95% CI, 1.41-4.25 ;P=0.001), disease progression during neoadjuvant chemotherapy (HR 2.24; 95% CI, 1.17-4.31 ;P=0.015) and perioperative RFA(HR 2.22; 95% CI, 1.21-4.05 ;P=0.010)] remained significant for OS (Table 3).

Discussion

This study is in accordance with recent studies in demonstrating that in the age group> 60 years, as we encounter more often non-surgical complications after liver resection for colorectal liver metastases and a decreased overall survival when compared to younger patients [4,7,11].

In most studies of surgical outcomes, the threshold used to define older patients is that of 70 years of age [22]. In the present study the threshold applied was that of 60 years of age and the reason for this, is that, from a medical perspective, this is the age when co-morbidities like coronary artery disease and other cardiovascular diseases become more prominent and frequent [11] and it approximates to the age of retirement in the UK which is around 63.8 years of age.

With regard to post liver resection complications, it has been demonstrated that the rate of complications was higher in senior patients as well as pre-operative administration of more than 4 cycles of systemic chemotherapy and major liver resection were shown to increase morbidity rates significantly. Multivariate analyses adjusted to age, sex, number of liver metastases, type of neoadjuvant cytotoxic chemotherapy, number of cycles of neoadjuvant chemotherapy and the extent of hepatectomy revealed that an age greater than 60 years and major hepatectomy were the only factors being independently related to influencing the perioperative morbidity (Table 3). Major surgical complications have been comparable between the two age groups; the rate of non-surgical complications though was higher in older patients. Schiergens et al also found that the prevalence of surgical complications in young patients and elderly patients undergoing liver resection (age groups <60, 60-69 and >70) was similar, with the non-surgical complications being significantly more frequent in the elderly group of patients [23]. Last but not least, there has been no difference in functional recovery of the liver, which was in accordance with the findings of Cook et al [16].

Regarding post-operative mortality, there was no difference between the two age groups. It should be highlighted that both patients from the elderly group died because of non-surgical complications, namely pneumonia and sepsis, whereas the one from the young group died because of liver insufficiency. This is partially consistent with the results of Sulpice et al, who also demonstrated that there was no difference in mortality rates between patients <60 years and those aged 60-74 years but there is a difference when compared to patients older than 75 years [4]. Our findings are also in agreement with those reported by Ide et al [24], who showed in a study of patients with HCC undergoing partial hepatectomy a similar mortality rate between young (<75) and elderly (>75) patients [24], and Menon et al, who demonstrated no substantial difference for patients more than 70 and less than 70 years of age after major hepatectomy [17]. Schiergens et al, on the other hand, showed that the thirty-day mortality rate was higher in elderly patients (>70 years of age) [23].

As far as disease free survival (DFS) and overall survival (OS) are concerned, univariate analyses failed to show an association between age greater than 60 years and DFS, but did demonstrate an association with OS (table 2); pre-, intra- and post-operatively RFA and disease progression during neoadjuvant chemotherapy that have also been associated with OS. In multivariate analysis, all variables related to reduced overall survival in the univariate analysis remained statistically significant. Regarding DFS, in the multivariate analysis, bilobar distribution of lesions and disease progression during neoadjuvant chemotherapy were statistically

Supplementary Table 1. *Post operative complications and their management.*

Variable		Age <60 N=110		Age>60 N=150		*P* Value
Type of complications		No=33	Management	No=64	Management	**0.037**
Wound		**7**		**12**		0.606
	Infection	6	5: Antibiotics 1: Debridement	8	6: Antibiotics 2: Debridement	0.966
	Dehiscence	1	Conservatively	4	3:Conservatively 1:Reoperation	0.400
Pulmonary		**5**		**15**		0.103
	Pleural effusion	4	3: Conservatively 1: Drainage	7	5: Conservatively 2: Drainage	0.746
	Pneumonia	1	Antibiotics	7	5:Antibiotics 2:Antibiotics plus mechanical ventilation	0.144
	Respiratory failure	0		1	Mechanical ventilation	0.999
Liver/biliary tree		**12**		**18**		0.786
	Bile leak	7	3: Conservatively* 4: Stent insertion	11	2: Conservatively* 9: Stent insertion	0.761
	Liver insufficiency	5	Conservatively	7	Conservatively	0.963
Intraabdominal Bleeding/ hematoma		**2**	2:Reopperation	**4**	1:Reopperation 2:Transfussion 1:Drainage	0.999
Cardiovascular		**4**		**11**		0.207
	Arrhythmia	2	Cardiovascular medication	5	4:Cardiovascular medication 1: Electrocardioversion	0.702
	Myocardial Infarction	1	ICU/organ support	3	ICU/organ support	0.640
	Hypertension	1	Cardiovascular medication	1		0.999
	Pericarditis	0		1	Conservatively	0.999
Bowel		**1**		**3**		0.640
	Anastomotic leak	1	Reoperation	1	Reoperation	0.999
	Ileus	0		2	Reoperation	0.510
Intraabdominal collections		**4**	2:Drainage 2:Conservatively	**5**	3:Drainage 2:Conservatively	0.999
Urinary tract infection		**0**		**1**	Antibiotics	0.999
DVT/PE		**1**	LMWH	**2**	1:LMWH 1:LMWH plus IVC Filter	0.999
Urinary bladder injury		**1**	Reoperation	**0**		0.423
Pseudomembranous colitis		**0**	Antibiotics	**1**	Antibiotics	0.999
Sepsis of unknown cause		**2**	Antibiotics	**2**	Antibiotics	0.999

LMWH: Low molecular weight heparin

important. This finding has been previously supported by Schiergens et al, who showed that overall survival was reduced in the elderly group of patients both in univariate and multivariate analyses [23], however, Menon et al reported no prominent difference in OS and DFS between patients more than 70 and less than 70 years of age undergoing

hepatectomy for CRLM [17] and that was also supported by Cescon et al [17, 25]. This could possibly be attributed to the fact that our age threshold has been different when compared to that used in other studies.

Sarcopenia, defined as the age-related loss of muscle leading of power, results in frailty and disability [26]. Epidemiological studies have attributed a rate of sarcopenia of 5–13% in the group age of 60–70 years and 11–50% in the group age of 80 years old [27,28]. Sarcopenia and frailty could count for additional factors affecting the postoperative course of patients above 60 years of age undergoing partial hepatectomy, as it has been reported to have a negative impact on the postoperative outcome after partial hepatectomy [29,30]. Dello et al have shown in a study of patients undergoing liver resection that sarcopenic patients had a disproportionally small preoperative total functional liver volume, when compared with the non-sarcopenic ones, meaning that the preoperative hepatic physiologic reserve is lower in the sarcopenic patients [31]. However, in their study age did not differ significantly between sarcopenia and non-sarcopenia groups [31].

Turrentine et al showed that advanced age itself remains a significant risk factor for postoperative morbidity and mortality [32]. On the other hand, other authors have reported that patients in the age group greater than 70 years of age are safe to undergo a major abdominal surgery such as a pancreatic resection, but they would need a life quality assessment prior to the procedure [33]. Furthermore, published studies support an increase of postoperative morbidity and mortality with advanced age [34-36]. Falch et al suggest that increased perioperative mortality in such patients may well correlate with the actual number of old patients undergoing emergency operations [35] whereas Neuman et al have shown that in the above group an increased mortality by postoperative of day 90 may be predicted by frailty [36].

In conclusion, one can understand from our study that an age greater than 60 years is associated with an increased rate of non-surgical complications and reduced overall survival in patients undergoing liver resection for colorectal liver metastases; It is important to perform a perioperative risk stratification, as well as a functional assessment in older patients undergoing partial hepatectomy, so that this group of patients can recover well in terms of morbidity and mortality as their younger counterparts.

Ethical Approval: *The authors declare that the study has been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.*

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