World J Surg (2012) 36:2161–2170
DOI 10.1007/s00268-012-1621-1
World Journal of Surgery

Right Hepatectomy in Patients over 70 Years of Age: An Analysis of Liver Function and Outcome

Emmanuel Melloul · Nermin Halkic · Dimitri Aristotle Raptis · Adrien Tempia · Nicolas Demartines

Published online: 1 May 2012

Abstract

Background As a consequence of the increase in life expectancy, hepatobiliary surgeons have to deal with an emerging aged population. We aimed to analyze the liver function and outcome after right hepatectomy (RH) in patients over 70 years of age.

Methods From January 2006 to December 2009, we prospectively collected data of 207 consecutive elective hepatectomies. In patients who had RH, cardiac risk was assessed by a dedicated preoperative workup. Liver failure (LF) was defined by the "fifty–fifty" criteria at postoperative day 5 (POD) and morbidity by the Clavien–Dindo classification. Liver function tests (LFTs) and short-term outcome were retrospectively analyzed in patients over (elderly group, EG) and younger (young group, YG) than 70 years of age.

Results Eighty-seven consecutive RH were performed during the study period. Indication for surgery included 90 % malignancy in 47 % of patients requiring preoperative chemotherapy. ASA grade > 2 (44 vs. 16 %, $p = 0.027$), ischemic heart disease (17 vs. 5 %, $p = 0.076$), and preoperative cardiac failure (26 vs. 2 %, $p < 0.001$) were more frequent in the EG ($n = 23$) than in the YG ($n = 64$). Both groups were similar regarding rates of normal liver parenchyma, chemotherapy and intraoperative parameters. The overall morbidity rates were comparable, but the serious complication (grades III–V) rate was relatively higher in the EG (39 vs. 25 %, $p = 0.199$), particularly in patients with diabetes mellitus (100 vs. 29 %, $p = 0.04$) and those who had additional nonhepatic surgery (67 vs. 35 %, $p = 0.110$) and transfusions (44 vs. 30 %, $p = 0.523$). The 90-day mortality rate was similar (9 % in the EG vs. 3 % in the YG, $p = 0.28$) and was related to heart failure in the EG. LFTs showed a similar trend from POD 1 to 8, and patients $\geq$70 years of age had no liver failure.

Conclusions Age $\geq$70 years alone is not a contraindication to RH. However, major morbidity is particularly higher in the elderly with diabetes. This high-risk group should be closely monitored in the postoperative course. Liver function is not altered in the elderly patient after RH.

E. Melloul · N. Halkic · A. Tempia · N. Demartines (✉)
Department of Visceral Surgery, University Hospital Lausanne (CHUV), Bugnon 46, 1012 Lausanne, Switzerland
e-mail: demartines@chuv.ch

E. Melloul
e-mail: emmanuel.melloul@chuv.ch

D. A. Raptis
Department of Visceral Surgery, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland

Introduction

Surgery in the elderly has become very common. In fact, due to increased life expectancy worldwide [1, 2], hepatobiliary (HPB) surgeons are dealing with an emerging aged population, which is expected to have a higher risk of postoperative complications and possibly adverse long-term outcomes. On the other hand, due to improvement in perioperative management, liver surgery is considered safe today [3], and several series have investigated the outcome of elderly patients after liver surgery [4–7]. These series assessed various indications and types of liver resection together and included patients with various underlying liver parenchyma. However, the cutoff for age was not always the same, with a few series using 65 years to define the elderly population, and others using 70 or even 75 [8–10].

The aging process is a biological reality but its influence on the function of organs like the liver remains controversial. Recently, comparable outcomes in graft failure and patient survival after transplantation of livers from donors older or younger than 70 years were reported, suggesting that liver function is not altered with age [11–14]. According to published data within the last decade [9, 10, 15, 16], minor liver resections (i.e., resections of <3 Couinaud's segment) can be performed safely in the elderly whatever the quality of the underlying parenchyma. In the case of right hepatectomy, the volume of the future liver remnant (FLR) and the quality of the underlying liver parenchyma are of primary concern for the postoperative outcome.

There is some evidence that major hepatectomy is well tolerated in older patients, however, the mortality risk ranges from 6 to 10 % in larger series [6, 8, 10, 17]. On the other hand, the data on the specific risks of right hepatectomy in patients over 70 years of age are scarce and lack standardization in terms of patient risk assessment, particularly for cardiac risk. In this setting, two questions are still debated about elderly patients and are the end points of our present study: (1) Are the functional reserve and regenerative capacity of the liver sufficient to tolerate a parenchymal reduction of 60 % or more? and (2) What is the impact of a right hepatectomy on postoperative cardiac function and patient outcome?

Patients and Methods

From January 2006 to December 2009, we prospectively collected all demographic, clinical, and laboratory data of patients who underwent elective liver resection in our tertiary referral university center. During the study period, all consecutive patients older (Elderly group, EG) and younger (Young group, YG) than 70 years old were assessed with a dedicated workup before undergoing right or extended right hepatectomy. Morbidity, mortality, and liver function were systematically recorded in both groups and data were analyzed retrospectively. The local ethics committee approved this study which was registered at ClinicalTrial.gov (NCT01471262).

Preoperative Assessment

All treatment strategies and indications for surgery were discussed by a multidisciplinary board. Before surgery, a senior HPB surgeon and an anesthetist assessed all patients in the outpatient clinic. The American Society of Anesthesiologists (ASA) grade was used to evaluate the patients' operative risk. Preoperative investigations included electrocardiogram and chest radiograph with blood sampling for all patients (white blood cell count, liver function tests, and creatinine levels). Preoperative cardiac risk assessment followed the guidelines for noncardiac surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anesthesiology (ESA) [18, 19]. Briefly, the diagnostic algorithm for risk stratification of myocardial infarction and left ventricular (LV) function was similar to that proposed for patients in the nonsurgical setting with known or suspected ischemic heart disease (IHD). Noninvasive testing included echocardiography, exercise electrocardiogram, or stress myocardial scintigraphy after assessment by a senior cardiologist from our institution. Invasive testing included coronary angiography with corrective intervention if necessary. Preoperative cardiac failure was defined as left ventricular ejection fraction of <50 % during echocardiography.

Prior to surgery, all patients had a high-resolution contrast-enhanced CT scan of the chest and abdomen. The aim of this imaging was to assess the liver volume, vascular anatomy, and the extent of the hepatic lesion and to rule out extrahepatic disease in cases of malignancy. If necessary, preoperative portal vein embolization (PVE) was performed according to the standard technique [20]. The indications for PVE included a future remnant liver volume <25 % in normal parenchyma, <30 % in cases of multiple cycles of chemotherapy (more than 6), and <40 % in cases of cirrhosis [21]. Patients with preoperative biliary obstruction and jaundice underwent percutaneous or endoscopic drainage prior to surgery. The following preoperative characteristics were also analyzed: renal function, obesity as defined by the World Health Organization (i.e., BMI $\geq$ 30 kg/m^2) [22], hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), and chemotherapy in patients with malignancy. Renal failure was defined preoperatively as creatinine clearance below 50 ml/min (Cockcroft formula) or if patients were under chronic hemodialysis.

Intraoperative Data

Liver resections were classified according to the Brisbane nomenclature [23]. Right hepatectomy was defined by the resection of liver Couinaud's segments V, VI, VII, and VIII, and extended right hepatectomy was defined by the resection of additional segments IV and/or I. Extended right hepatectomy was indicated in patients with an extensive tumor or vascular invasion. The surgical procedure included parenchyma transection using an ultrasonic dissector, and intermittent pedicle clamping without preconditioning (Pringle maneuver) was reserved only for the cases of bleeding. Hemostasis was achieved with bipolar coagulation, hemoclips, and ligatures.

During parenchymal transection the central venous pressure was maintained below 5 cmH_2O to prevent venous hemorrhage and cardiac overload. The following intraoperative data were also collected: additional nonhepatic surgery, intermittent clamping duration, total venous exclusion of the liver (TVE), need for transfusion, and operative duration.

Postoperative Care and Outcome Analysis

All patients who underwent a right or extended right hepatectomy were transferred postoperatively to the intensive care unit (ICU) or to the surgical intermediate care unit of our hospital. This was first to maintain the fluid balance, second for cardiac monitoring, and third for respiratory management. Postoperative morbidity was assessed using the validated classification system by Clavien–Dindo [24]. Serious complications were categorized as grades III–V and defined as morbidity requiring surgical or radiological intervention (under local or general anesthesia), ICU transfer with single- or multiple-organ failure, or death. In addition, the following specific liver complications were recorded: postoperative ascites, biliary leak, and liver failure. Postoperative transaminase (AST and ALT) levels, total bilirubin (TB) levels, and prothrombin time (PT) were recorded daily until postoperative day (POD) 8. Liver failure was defined as a bilirubin level of more than 50 mmol/l and prothrombin index <50 % of normal value at POD 5 according to the "fifty–fifty" criteria [25]. Postoperative pulmonary morbidity was also analyzed, including pulmonary embolism (PE), lung infection requiring intravenous antibiotic therapy with or without invasive ventilatory support, and pleural effusion requiring drainage. Postoperative mortality was defined as any death occurring within 90 days after surgery.

Histopathological Analysis

All liver specimens were sent for histopathological assessment after surgery. A specialized hepatobiliary pathologist analyzed the liver lesions and the quality of the underlying parenchyma. The extent of parenchyma fibrosis was assessed with the Metavir score [26]. Liver steatosis was categorized into two groups: less than or more than 30 % micro- or macrovesicular steatosis [27, 28]. Liver parenchyma with a fibrosis score of F0–F2 and/or with <30 % steatosis was considered "normal" [28].

Statistical Analysis

The Fisher exact test or the χ^2 test was used for categorical variables and the Student *t* test or one-way ANOVA was used for continuous variables where appropriate. The results were expressed as mean and standard deviation (SD) or median and range. The current clinical relevant risk factors for major postoperative complications (grade III–V) in the elderly (i.e., ASA grade, preoperative renal and cardiac failure, ischemic heart disease, diabetes, obesity, hypertension, transfusion, additional surgery, and chemotherapy) were included in the univariate analysis and proportions were compared according to the two age groups (≥ or <70 years old). Statistical analyses were performed using SPSS for Windows v18 (SPSS Inc., Chicago, IL). Statistical significance was accepted as $p < 0.05$ (2-sided tests).

Results

During the study period, a total of 207 consecutive patients who underwent hepatectomy were collected in the database, including 87 right or extended right hepatectomies, which correspond to the study cohort (Fig. 1). The median age was 60 years (range = 21–85) and the male/female ratio was 55/32. Additional nonhepatic surgery was required in 33 % of the patients. The main indication for surgery was malignancy in 90 % ($n = 78$), including 47 % who underwent preoperative chemotherapy. Liver parenchyma was normal in 78 % of the specimens and the overall liver failure rate was 5 %. Overall, postoperative morbidity and 90-day mortality rates were 29 % and 4.6 %, respectively.

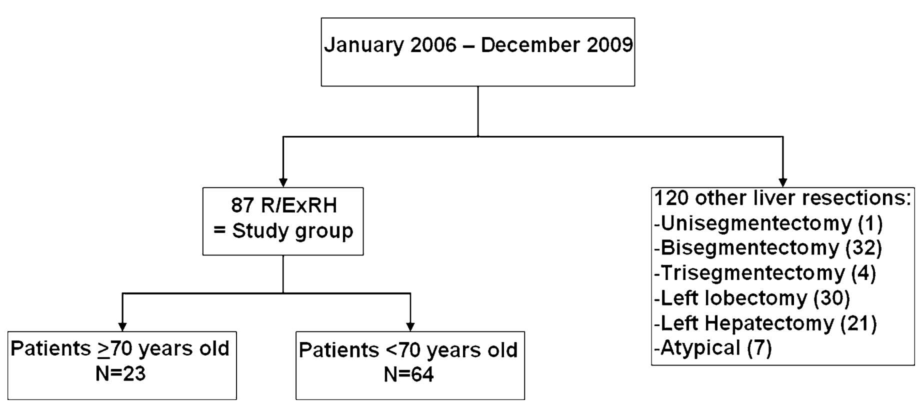

Fig. 1 Study population

Demographic Characteristics of Patients Younger and Older than 70 years

Twenty-six percent of the patients ($n = 23$) were older than 70 years of age. In the EG versus the YG, preoperative characteristics were comparable, except for the ASA grade, cardiac failure, and IHD rates, which were higher in the EG (Table 1). Of note, two patients (9 %) in the EG required cardiac angiography with dilatation due to significant coronary artery stenosis diagnosed in the preoperative workup. Indication for surgery was mainly malignancy in both groups (95 vs. 88 %, $p = 0.434$), and the rate of preoperative chemotherapy was similar. In hepatocellular carcinoma (HCC) patients ($n = 21$), hepatitis B serology was positive in one patient >70 years old and in four patients <70 years old. Hepatitis C serology was negative in all patients >70 years old and positive in one patient <70 years old. As listed in Table 2, operating time was not different, with a median of 300 min [interquartile range (IQR) = 230–370] in the EG versus 270 min (IQR = 225–348) in the YG ($p = 0.490$). Total intermittent clamping was also not different, with a median of 16 min in the EG (IQR = 0–30) versus 23 min in the YG (IQR = 0–40) ($p = 0.565$). The rate of additional nonhepatic surgery was similar between the two groups (26 % in the EG vs. 36 % in the YG, $p = 0.391$) and was always necessary due to local tumor extension. The need for transfusion was 39 % in the EG versus 42 % in the YG ($p = 0.798$). Table 3 summarizes the postoperative outcomes. The overall complication rate was not different between the elderly and young patients, but for grades III–V morbidity tended to be higher in the EG (39 vs. 25 %, $p = 0.199$). Of note, there were more cardiac complications but no liver failures in the EG. The rates of liver- and pulmonary-related complications were not different between the two groups. The median hospital stay for the EG was of 17 days (IQR = 13–29) compared with 15 days (IQR = 11–22) for the YG ($p = 0.363$), and the 90-day mortality rate was 9 versus 3 % ($p = 0.281$), respectively. The two deaths in the EG were due to heart failure. The first fatality was a patient with an ASA grade of III, cardiac insufficiency, and IHD, and the second was an ASA III patient with diabetes but with no previous history of cardiac disease and a normal preoperative cardiac workup. In the YG, the two deaths were related to liver failure leading to multiple-organ failure in the context of cirrhosis. These two patients were 59 and 63 years old, obese (BMI = 32 and 31, respectively) and with an ASA grade of III. They both developed HCC secondary to alcohol-induced cirrhosis and nonalcoholic steatohepatitis (biopsy-proven), respectively. Serologies for hepatitis B and C were negative in both cases. Of note, the second patient had preoperative transarterial chemoembolization (TACE) followed by PVE due to a large tumor size (7.5 × 6 cm diameter). Finally, the future liver remnant volume was 38 and 40 % of the total initial liver volume on the preoperative

Table 1 Demographic characteristics of patients

	≥70 years ($N = 23$)	<70 years ($N = 64$)	*P* value	Odds ratio	95 % CI
Male/female ratio (*n*)	16/7	42/22	0.41		
Median age (range)	75 (70–85)	57 (21–66)	<0.001		
ASA grade			0.027	4.1	1.4–12
I	4 %	6 %			
II	52 %	78 %			
III	44 %	16 %			
Comorbidities					
Renal failure	9 %	3 %	0.274	2.94	0.4–22
Cardiac failure	26 %	2 %	0.001	22.2	2.5–200[b]
Ischemic heart disease	17 %	5 %	0.076	4.3	0.9–21
COPD	13 %	3 %	0.113	4.6	0.7–29
Diabetes	13 %	11 %	0.72	1.22	0.3–5.2
Hypertension	35 %	34 %	1.0	1.02	0.4–2.8
Obesity	17 %	12 %	0.725	1.47	0.4–5.5
Portal vein embolization	52 %	45 %	0.631	1.31	0.5–3.4
Malignant disease[a]	95 %	88 %	0.434		
Preoperative chemotherapy	30 %	49 %	0.145	0.4	0.2–1.2

CI confidence interval, *COPD* chronic obstructive pulmonary disease

[a] Hepatocellular carcinoma ($n = 21$), colorectal liver metastases ($n = 35$), cholangiocarcinoma ($n = 8$), gallbladder cancer ($n = 1$), other metastases ($n = 10$)

[b] In small numbers, it is common to have overestimated odds ratio. This result should be taken with caution

Table 2 Intraoperative data

	≥70 years (%) ($N = 23$)	<70 years (%) ($N = 64$)	p value	Odds ratio	95 % CI
Additional nonhepatic surgery	6 (26)	23 (36)	0.391	0.62	0.2–1.8
Hepaticojejunal anastomosis	4	11			
Colectomy	1	1			
Diaphragmatic resection	1	5			
Vena cava resection	0	1			
Portal vein resection	0	1			
Other[a]	0	3			
Operative time	300 (IQR 230–370)	270 (IQR 225–348)	0.490	–	–
Pedicular clamping	13(65)	41(66)	1.000	0.95	0.3–2.7
Need for transfusions	9(39)	27(42)	0.798	0.88	0.3–2.3

[a] Adrenalectomy (1), nephrectomy (1), pulmonary wedge resection (1)

Table 3 Postoperative outcome

	≥70 years (%) ($N = 23$)	<70 years (%) ($N = 64$)	p value	Odds ratio	95 % CI
Minor morbidity (grade I–II)[a]	3 (13)	8 (12.5)	1.0	1.05	0.2–4.3
Major morbidity (grade III–V)[a]	9 (39)	16 (25)	0.19	1.92	0.7–5.3
Liver failure[b]	0	3			
Laparotomy (biliary peritonitis/bowel perforation)	2	3			
Biliary leak	3	5			
ARDS	1	1			
Cardiac failure	2	0			
Myocardial infarction	1	1			
Empyema	0	1			
Acute portal vein thrombosis	0	2			
Ascites	4 (18)	8 (13)	0.50	1.5	0.4-5.6
Overall biliary leak	3 (14)	11 (17)	1.00	0.76	0.2-3.0
Overall liver failure rate	0	4 (6)	0.57	NA[c]	NA[c]
Overall pulmonary complications	3 (14)	14 (22)	0.54	0.55	0.1–2.1
90-day mortality	2 (9)	2 (3)	0.28	3	0.4–23
Total hospital stay (days)	17 (IQR = 13–29)	15 (IQR = 11–22)	0.36	–	–

[a] According to Clavien–Dindo classification [24]

[b] According to the "fifty–fifty" criteria at POD 5 [25]

[c] Odds ratio could not be calculated because of the presence of a zero in the variables

CT scan for EG and YG, respectively. Surgery was uneventful; however, in two patients a diaphragmatic resection was required due to tumor invasion. In the postoperative course, both patients had liver failure according to the "fifty–fifty" criteria, complicated by infected ascites, ventilator-associated pneumonia, and hepatorenal syndrome. Despite supportive care in the ICU with renal replacement therapy, both patients died from multiple-organ failure at days 15 and 31, respectively. In both cases, the nontumoral liver parenchyma analysis showed cirrhosis with microvesicular steatosis of more than 40 %.

Additional univariate analysis assessing the factors associated with major postoperative complications showed that patients older than 70 years and with diabetes were particularly at risk for grade III–V complications (Table 4). In this setting major morbidity was related to one cardiac failure, one ischemic colon perforation, and one biliary peritonitis secondary to Roux-en-Y leakage. Of note, there was a trend toward higher major complications in the elderly who had additional nonhepatic surgery versus those who did not (67 vs. 35 %, $p = 0.110$) and transfusions (44 vs. 30 %, $p = 0.523$).

Table 4 Analysis of predictors for postoperative major morbidity (grades III–V according to the Clavien–Dindo classification [24])

Variable	Age group	No. of patients	No. complications [*N* (%)]	Grades III–V complications [*N* (%)]	*p* value	Odds ratio	95 % CI
ASA > 2	≥70	10	4 (40)	6 (60)	0.1	2.62	0.45–15.31
	<70	11	7 (64)	4 (36)			
Preoperative renal failure	≥70	2	1 (50)	1 (50)	0.49	1	0.02–50.4
	<70	2	1 (50)	1 (50)			
Preoperative cardiac failure	≥70	6	3 (50)	3 (50)	0.49	NA[a]	NA[a]
	<70	0	0	0			
IHD	≥70	4	3 (75)	1 (25)	0.53	0.67	0.02–18
	<70	3	2 (67)	1 (33)			
Diabetes	≥70	3	0	3 (100)	0.04	NA[a]	NA[a]
	<70	7	5 (71)	2 (29)			
Obesity	≥70	2	2 (50)	2 (50)	0.59	3	0.24–37.7
	<70	8	6 (75)	2 (25)			
Hypertension	≥70	8	3 (38)	5 (62)	0.17	4.4	0.8–24.6
	<70	22	16 (73)	6 (27)			
Transfusion	≥70	9	5 (56)	4 (44)	0.52	1.9	0.4–9
	<70	27	19 (70)	8 (30)			
Additional surgery	≥70	6	2 (33)	4 (67)	0.11	6.7	1.04–43.9
	<70	23	15 (65)	8 (35)			
Chemotherapy	≥70	7	5 (71)	2 (29)	0.4	1.6	0.24–10.4
	<70	30	24 (80)	6 (20)			

IHD ischemic heart disease, *CI* confidence interval

[a] Odds ratio could not be calculated because of the presence of a zero in the variables

Analysis of Liver Function

Liver function tests had a similar trend in both groups throughout PODs 1–8. At POD 1 versus 8, the median total bilirubin level was 26 (IQR = 20–43) versus 26 (IQR = 12–35) mmol/l in the EG and 33 (IQR = 26–55) versus 21 (IQR = 11–50) mmol/l in the YG, respectively ($p = 0.10$ and 0.89) (Fig. 2). Similarly, the median prothrombin time was 60 (IQR = 55–70) versus 83 (IQR = 70–90) s in the EG and 60 (IQR = 50–65) versus 85 (IQR = 70–100) s in the YG ($p = 0.1$ vs. 0.36, respectively) (Fig. 3). Finally, only ALT levels were significantly higher at POD 1 and 3 in the YG (median = 413 vs. 275 mmol/l and 244 vs. 174 mmol/l, $p = 0.046$ and $p = 0.048$, respectively).

Histopathological Analysis

In the elderly versus the young patients, the analysis of perilesional liver parenchyma showed a similar rate of normal parenchyma (78 % in both groups, $p = 0.991$), with similar rates of F3–F4 fibrosis (22 vs. 19 %, $p = 0.762$) and macrovesicular steatosis ≥30 % (9 vs. 5 %, $p = 0.480$).

Discussion

The results of our study suggest that age over 70 years alone is not a contraindication to right hepatectomy. Surgery did not increase the in-hospital mortality when compared to younger patients, and the functional reserve of the "old liver" was not altered. However, major morbidity was higher in the elderly with diabetes.

Within the last decade, most studies reporting complications of patients who underwent a hepatectomy included both major and minor resections, without providing a subgroup analysis (Table 5). To date, four retrospective series [6, 8, 10, 17] investigated the outcome of elderly patients after major hepatectomy. However, it is difficult to interpret their results for three reasons. First, the preoperative workup used to assess elderly patients was neither stated nor standardized. Second, the type of major hepatectomy performed was varied and multiple (i.e., it included right and/or left hepatectomies). Third, the cutoff for age was not always the same (range = 60–75). Our study provides a homogeneous series of consecutive patients older and younger than 70 years of age who underwent a standardized risk assessment workup before formal right hepatectomy. As expected, elderly patients had more

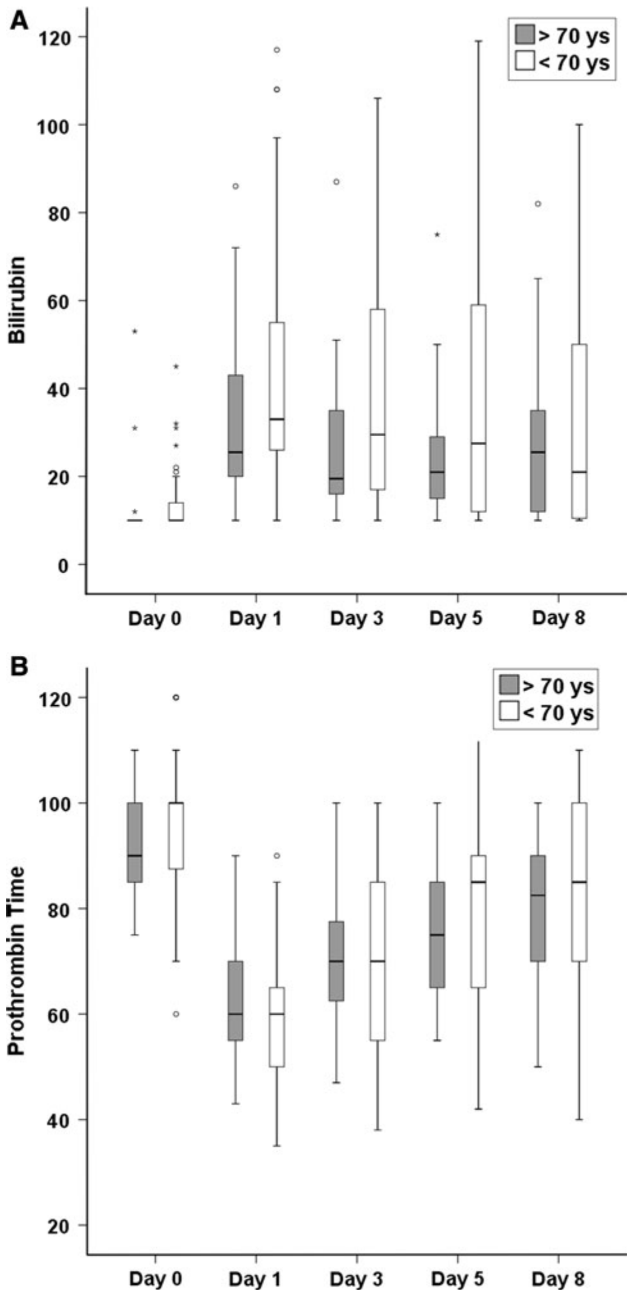

Fig. 2 Median total bilirubin level (mmol/l) (**a**) and prothrombin time (s) (**b**) from postoperative day 1–8 in patients younger and older than 70 years of age after right hepatectomy

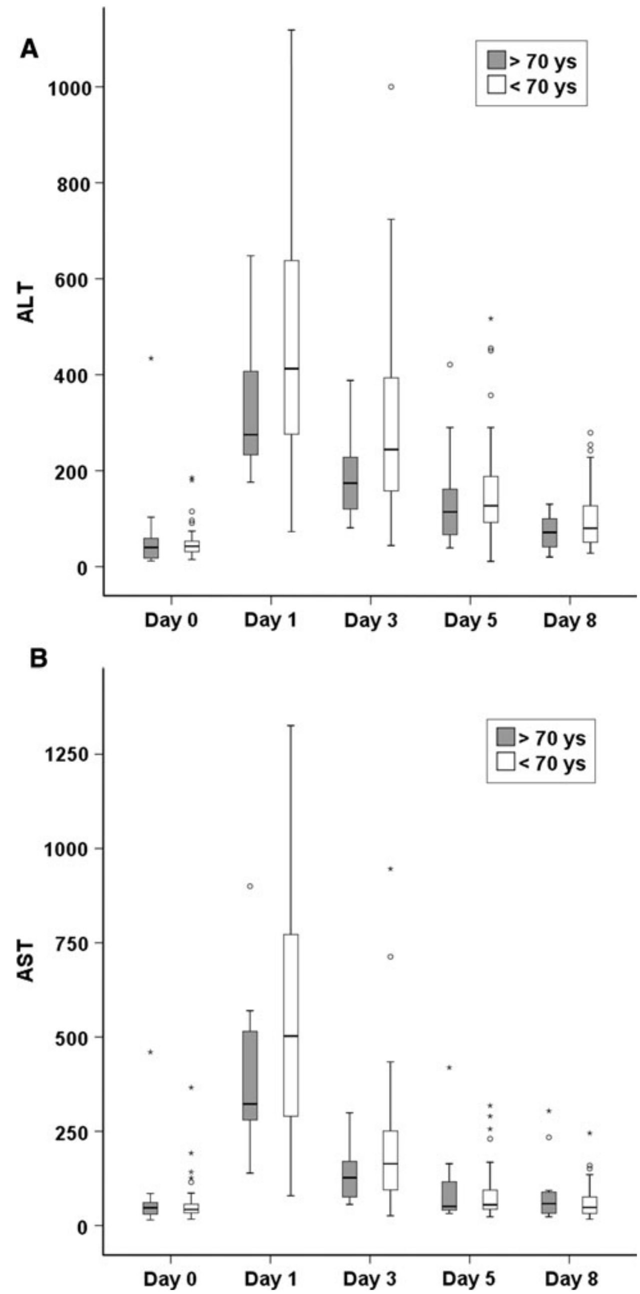

Fig. 3 Median ALT (mmol/l) (**a**) and AST (mmol/l) (**b**) levels from postoperative day 1 to 8 in patients younger and older than 70 years of age after right hepatectomy

cardiac comorbidities. Nevertheless, their 90-day mortality rate was not different than that of younger patients and was in accordance with the 0–10 % reported rates after major hepatectomy [5, 6, 8–10, 15, 17]. Of note, the dedicated workup allowed us to correct potential life-threatening cardiac disease before hepatic surgery in nearly 10 % of the elderly patients. Formerly, the most frequently reported causes of death in the elderly without any underlying disease were hepatic failure, myocardial infarction, renal failure, pneumonia, and gastrointestinal bleeding [29–31]. Currently, monitoring a low central venous pressure during hepatic transection with intraoperative fluid restriction allowed the reduction of the risk of congestive heart failure and arrhythmias, which are the most dangerous complications encountered after major liver resections in the elderly [8, 10].

Surprisingly, despite the dedicated preoperative workup and a low central venous pressure maintained during right hepatectomy in our patients, death was always related to postoperative cardiac failure in the elderly group.

Table 5 Series of hepatectomies in elderly within the past 10 years

Authors [ref]	Elderly (total)	Age (years)	Main indications	Right hepatectomy rate	Complication rate (%)	Mortality rate (%)
Brand et al. [44]	41	>70	CLM	Unknown	39 %	7 %
Hanazaki et al. [5]	103	>70	HCC	10 %	28 %	10 %
Ettorre et al. [8]	24	>65	HCC, CLM	100 %	12 %	4 %
Aldrighetti et al. [9]	32	>70	HCC, CLM	34 %	9 %	0
Cescon et al. [17]	23	>70	Multiple	100 %	39 %	0
Yeh et al. [15]	34	>70	HCC	Unknown	Unknown	8 %
Ferrero et al. [16]	64	>70	HCC	31 %	23 %	3 %
Menon et al. [6]	127	>70	CLM	70 %	31 %	8 %
Adam et al. [7]	1624	>70	CLM	Unknown	38 %	4 %
Reddy et al. [10]	322	>65	Multiple	62 %	47 %	6 %
Present study, 2011	23	>70	CLM, HCC	100 %	39 %	9 %

CLM colorectal liver metastases, *HCC* hepatocellular carcinoma

These results matched those of other published studies [3, 8] and may be explained by the limited predictive value of left ventricular (LV) function assessment for perioperative outcome [19]. Indeed, LV failure predicts with a sensitivity of 50 % the risk of perioperative nonfatal myocardial infarction or cardiac death after noncardiac surgery [32]. These results suggest that cardiac risk after right hepatectomy in the elderly should not be underestimated, even with normal preoperative workup, and that our method of cardiac assessment should not be withheld but it needs revision.

After major hepatectomy in the elderly, the reported complication rate ranges from 30 to 50 % [6, 7, 10]. In our study, overall morbidity was comparable between the young and elderly groups. Pulmonary complications were not different, confirming what was found in previous reports [17]. This may be explained by the routine use of postoperative respiratory management and intraoperative fluid restriction. On the other hand, 39 % of the morbidity observed in our elderly patients referred to grade III–V complications. Except of the two cardiac failures that led to death, all other complications could be managed with ICU support, surgery, or endoscopic treatment, without affecting the length of in-hospital stay. Interestingly, patients over 70 years of age and with diabetes had a significantly increased risk for major complications. It is acknowledged that patients with diabetes are more prone to sepsis, atherosclerosis, and delayed healing [33]. In addition, patients with diabetes were associated with delayed ventilator weaning, more transfusions, and greater morbidity after liver resections [33, 34]. According to our results, the morbidity risk after right hepatectomy in patients with diabetes seems to be amplified by the aging process. We can speculate that vascular lesions induced by both factors may be involved in this risk, since most major complications had an ischemic etiology. As reported by others [3, 6, 35–37], there was also a trend toward higher morbidity in the elderly who had additional nonhepatic surgery or transfusions.

Thus, there is a potentially greater risk for major complications after right hepatectomy in the elderly, but this morbidity is still acceptable for two reasons: (1) most patients were operated on for malignancy (>90 % HCC and colorectal liver metastases) and required a right hepatectomy to obtain a tumor-free margin, and (2) most complications were managed in the same way as in younger patients, without increasing the mortality risk or the length of hospital stay. Of note, 33-50 % of the patients with colorectal liver metastases were older than 70 years [7]. Moreover, liver resection offers a similar 5-year survival as that in younger patients [7, 38, 39]. These results were also confirmed in elderly patients with HCC [15, 16]. Therefore, surgery in the aged population should yield the same oncological results as in younger patients. To achieve this goal, a right or extended right hepatectomy may be necessary. An accepted policy to reduce the postoperative morbidity in these patients is then to avoid additional nonhepatic surgery and transfusion whenever possible. Finally, elderly patients with diabetes should have a dedicated preoperative workup and should be closely monitored postoperatively to anticipate fatal complications, mainly related to heart failures.

The aging process of the liver is still not fully understood and involves several changes in the liver architecture. For example, the size of the liver and the sinusoidal flow decrease with age [40, 41], but their influence on liver function remains unclear. In our study, the rate of normal liver parenchyma was similar in patients older and younger than 70 years of age, suggesting that liver steatosis or fibrosis was not increase with age. Moreover, liver function tests had a similar trend throughout POD 1–8, confirming the results reported by Ettorre et al. [8] in patients over 65 years old. We added the "fifty–fifty" criteria [25] to show that the postoperative liver failure rate was not increased in patients over 70 years old, provided that liver parenchyma was prepared by PVE and biliary drainage when required. These results support the hypothesis that liver function is not significantly altered with age.

One of the limitations of this study is the small sample size of elderly patients; however, the incidence of right hepatectomy in patients over 70 years old is extremely low in many centers. Another limitation is that in the preoperative workup, we did not use (at that time) the indocyanine green (ICG) retention test [42, 43]. This test, widely used in Asian countries and some centers in Europe to assess liver function, may contribute further to assessing the postoperative outcome of patients who will undergo a right hepatectomy as it may correlate with the liver volume. Well-designed prospective multicenter trials that include the ICG retention test in the preoperative workup may further confirm our findings.

In conclusion, the present study confirms that right hepatectomy can be performed safely in patients over 70 years of age without increased morbidity, provided a careful cardiac and liver parenchyma assessment is performed. However, the major morbidity will be higher in elderly patients with diabetes and will tend to increase in those who need additional nonhepatic surgery or blood transfusions. Finally, age does not alter significantly the postoperative functional reserve of the liver. A similar analysis remains to be performed in patients above 80 years of age.

Conflict of Interest All the authors declare that they have not received any funding from any individual or company to carry out this study.

References

1. Arias E (2004) National Vital Statistics Reports vol. 52, No. 14 (DHHS Publication No. (PHS) 2004–1120). http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_14.pdf. Accessed Jan 2011
2. European Commission. Eurostat statistics. http://epp.eurostat.ec.europa.eu/portal/page/portal/product_details/publication?p_product_code=KS-CD-11-001. Accessed Jan 2011
3. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK et al (2004) Improving perioperative outcome expands the role of hepatectomy in management of benign and malignant hepatobiliary diseases: analysis of 1222 consecutive patients from a prospective database. Ann Surg 240(4):698–708 (discussion 708–710)
4. Poon RT, Fan ST, Lo CM, Liu CL, Ngan H, Ng IO et al (1999) Hepatocellular carcinoma in the elderly: results of surgical and nonsurgical management. Am J Gastroenterol 94(9):2460–2466
5. Hanazaki K, Kajikawa S, Shimozawa N, Shimada K, Hiraguri M, Koide N et al (2001) Hepatic resection for hepatocellular carcinoma in the elderly. J Am Coll Surg 192(1):38–46
6. Menon KV, Al-Mukhtar A, Aldouri A, Prasad RK, Lodge PA, Toogood GJ (2006) Outcomes after major hepatectomy in elderly patients. J Am Coll Surg 203(5):677–683
7. Adam R, Frilling A, Elias D, Laurent C, Ramos E, Capussotti L et al (2010) Liver resection of colorectal metastases in elderly patients. Br J Surg 97(3):366–376
8. Ettorre GM, Sommacale D, Farges O, Sauvanet A, Guevara O, Belghiti J (2001) Postoperative liver function after elective right hepatectomy in elderly patients. Br J Surg 88(1):73–76
9. Aldrighetti L, Arru M, Caterini R, Finazzi R, Comotti L, Torri G et al (2003) Impact of advanced age on the outcome of liver resection. World J Surg 27(10):1149–1154. doi:10.1007/s00268-003-7072-y
10. Reddy SK, Barbas AS, Turley RS, Gamblin TC, Geller DA, Marsh JW et al (2011) Major liver resection in elderly patients: a multi-institutional analysis. J Am Coll Surg 212(5):787–795
11. Borchert DH, Glanemann M, Mogl M, Langrehr J, Neuhaus P (2005) Adult liver transplantation using liver grafts from donors over 70 years of age. Transplant Proc 37(2):1186–1187
12. Grazi GL, Cescon M, Ravaioli M, Ercolani G, Pierangeli F, D'Errico A et al (2001) A revised consideration on the use of very aged donors for liver transplantation. Am J Transplant 1(1):61–68
13. Gastaca M, Valdivieso A, Pijoan J, Errazti G, Hernandez M, Gonzalez J et al (2005) Donors older than 70 years in liver transplantation. Transplant Proc 37(9):3851–3854
14. Borchert D, Glanemann M, Mogl M, Langrehr JM, Neuhaus P (2005) Older liver graft transplantation, cholestasis and synthetic graft function. Transplant Int 18(6):709–715
15. Yeh CN, Lee WC, Jeng LB, Chen MF (2004) Hepatic resection for hepatocellular carcinoma in elderly patients. Hepatogastroenterology 51(55):219–223
16. Ferrero A, Vigano L, Polastri R, Ribero D, Lo Tesoriere R, Muratore A et al (2005) Hepatectomy as treatment of choice for hepatocellular carcinoma in elderly cirrhotic patients. World J Surg 29(9):1101–1105. doi:10.1007/s00268-005-7768-2
17. Cescon M, Grazi GL, Del Gaudio M, Ercolani G, Ravaioli M, Nardo B et al (2003) Outcome of right hepatectomies in patients older than 70 years. Arch Surg 138(5):547–552
18. Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G et al (2009) Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. Eur Heart J 30(22):2769–2812
19. Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G et al (2010) Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). Eur J Anaesthesiol 27(2):92–137
20. Madoff DC, Abdalla EK, Vauthey JN (2005) Portal vein embolization in preparation for major hepatic resection: evolution of a new standard of care. J Vasc Interv Radiol 16(6):779–790
21. Clavien PA, Petrowsky H, DeOliveira ML, Graf R (2007) Strategies for safer liver surgery and partial liver transplantation. N Engl J Med 356(15):1545–1559
22. World Health Organization (1995) Physical status: the use and the interpretation of anthropometry. Report of a WHO expert committee. Technical Report Series No. 854. World Health Organization, Geneva, pp 1–452
23. Strasberg SM (2005) Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. J Hepatobiliary Pancreat Surg 12(5):351–355
24. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD et al (2009) The Clavien–Dindo classification of

surgical complications: five-year experience. Ann Surg 250(2): 187–196
25. Paugam-Burtz C, Janny S, Delefosse D, Dahmani S, Dondero F, Mantz J et al (2009) Prospective validation of the "fifty–fifty" criteria as an early and accurate predictor of death after liver resection in intensive care unit patients. Ann Surg 249(1): 124–128
26. Bedossa P, Poynard T (1996) An algorithm for the grading of activity in chronic hepatitis C. The METAVIR Cooperative Study Group. Hepatology 24(2):289–293
27. D'Alessandro AM, Kalayoglu M, Sollinger HW, Hoffmann RM, Reed A, Knechtle SJ et al (1991) The predictive value of donor liver biopsies on the development of primary nonfunction after orthotopic liver transplantation. Transplant Proc 23(1 Pt 2): 1536–1537
28. McCormack L, Petrowsky H, Jochum W, Furrer K, Clavien PA (2007) Hepatic steatosis is a risk factor for postoperative complications after major hepatectomy: a matched case-control study. Ann Surg 245(6):923–930
29. Fortner JG, Lincer RM (1990) Hepatic resection in the elderly. Ann Surg 211(2):141–145
30. Fong Y, Brennan MF, Cohen AM, Heffernan N, Freiman A, Blumgart LH (1997) Liver resection in the elderly. Br J Surg 84(10):1386–1390
31. Melendez J, Ferri E, Zwillman M, Fischer M, DeMatteo R, Leung D et al (2001) Extended hepatic resection: a 6-year retrospective study of risk factors for perioperative mortality. J Am Coll Surg 192(1):47–53
32. Kertai MD, Boersma E, Bax JJ, Heijenbrok-Kal MH, Hunink MG, L'Talien GJ et al (2003) A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart 89(11):1327–1334
33. Gedaly R, McHugh PP, Johnston TD, Jeon H, Ranjan D, Davenport DL (2009) Obesity, diabetes, and smoking are important determinants of resource utilization in liver resection: a multicenter analysis of 1029 patients. Ann Surg 249(3):414–419
34. Guckelberger O, Thelen A, Benckert C, Schoebel C, Reuter S, Klupp J et al (2006) Diabetes mellitus is no independent risk factor for perioperative mortality following hepatic resection. Exp Clin Endocrinol Diabetes 114(5):257–261
35. Cescon M, Vetrone G, Grazi GL, Ramacciato G, Ercolani G, Ravaioli M et al (2009) Trends in perioperative outcome after hepatic resection: analysis of 1500 consecutive unselected cases over 20 years. Ann Surg 249(6):995–1002
36. Belghiti J, Hiramatsu K, Benoist S, Massault P, Sauvanet A, Farges O (2000) Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. J Am Coll Surg 191(1):38–46
37. Lordan JT, Riga A, Worthington TR, Karanjia ND (2009) Early and long-term outcomes of patients undergoing liver resection and diaphragm excision for advanced colorectal liver metastases. Ann R Coll Surg Engl 91(6):483–488
38. Zacharias T, Jaeck D, Oussoultzoglou E, Bachellier P, Weber JC (2004) First and repeat resection of colorectal liver metastases in elderly patients. Ann Surg 240(5):858–865
39. Turrini O, Guiramand J, Moutardier V, Viret F, Bories E, Giovannini M et al (2005) Major hepatectomy for metastasis of colorectal cancer improves survival in the elderly. Ann Chir 130(9):562–565
40. Furrer K, Rickenbacher A, Tian Y, Jochum W, Bittermann AG, Kach A et al (2011) Serotonin reverts age-related capillarization and failure of regeneration in the liver through a VEGF-dependent pathway. Proc Natl Acad Sci USA 108(7):2945–2950
41. Le Couteur DG, Cogger VC, Markus AM, Harvey PJ, Yin ZL, Ansselin AD et al (2001) Pseudocapillarization and associated energy limitation in the aged rat liver. Hepatology 33(3):537–543
42. Makuuchi M, Kosuge T, Takayama T, Yamazaki S, Kakazu T, Miyagawa S et al (1993) Surgery for small liver cancers. Semin Surg Oncol 9(4):298–304
43. Torzilli G, Makuuchi M, Inoue K, Takayama T, Sakamoto Y, Sugawara Y et al (1999) No-mortality liver resection for hepatocellular carcinoma in cirrhotic and noncirrhotic patients: is there a way? A prospective analysis of our approach. Arch Surg 134(9):984–992
44. Brand MI, Saclarides TJ, Dobson HD, Millikan KW (2000) Liver resection for colorectal cancer: liver metastases in the aged. Am Surg 66(4):412–415 (discussion 5–6)