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Laparoscopic major hepatectomy for colorectal liver metastases in elderly patients: a single-center, case-matched study

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Abstract

Background The incidence of colorectal cancer liver metastases (CRLM) among elderly patients has increased; therefore, older patients are increasingly being considered for hepatic resection. However, data regarding the outcome of laparoscopic major hepatectomy (LMH) in elderly patients are limited. The aim of this study was to evaluate the safety and feasibility of LMH in elderly patients with CRLM.

Methods From January 1998 to September 2013, a total of 31 patients aged ≥70 years (elderly group) were matched with 62 patients <70 years (young group) by demographics, tumor characteristics, and details of surgical procedures.

Results The elderly group was characterized by a higher incidence of hypertension (41.9 vs. 17.7 %, $P = 0.022$), ≥2 comorbidities (32.3 vs. 11.3 %, $P = 0.021$), and lower prevalence of metastatic rectal cancer (12.9 vs. 38.7 %, $P = 0.015$). Intraoperative variables, such as surgical duration (300 vs. 240 min, $P = 0.920$), blood loss (400 vs. 300 mL, $P = 0.361$), and transfusion rate (9.7 vs. 12.9 %, $P = 0.726$), were not notably different between the groups. Postoperative mortality (0 vs. 0 %), complications (54.8 vs. 41.9 %, $P = 0.276$), and major complications (27.4 vs. 16.1 %, $P = 0.303$, respectively) were comparable between the groups. The 3-year overall survival rates were 61.7 % in the young group (median 40 months) and 57.9 % in the elderly group (median 39 months), respectively ($P = 0.842$).

Conclusions Our results clearly demonstrated that LMH for CRLM could be safely performed in elderly patients; thus, advanced age itself should not be regarded as a contraindication for LMH.

Keywords Laparoscopic liver resection · Major hepatectomy · Elderly patients

Among industrialized countries, the population older than 80 years has continuously increased during the last century and nearly 9 % of the French population was older than 75 years in 2010 [1]. Meanwhile, the rising incidence of colorectal cancer liver metastases (CRLM) has also resulted in a dramatic increase in the number of elderly patients considered for hepatic resection. However, elderly patients represent only 10–20 % of those considered for surgery [2], reflecting a high proportion of patients contraindicated for curative treatment. Indeed, elderly patients present more frequently with comorbidities, particularly cardiovascular and pulmonary diseases, with an incidence of 20–27 and 14 %, respectively [3]; thus, the benefit-to-risk ratio continues to leave many clinicians reluctant to propose major liver resection (i.e., resection of ≥3 segments) for treatment of elderly patients. However, advances in hepatic surgery and perioperative care have reduced age-related contraindications for liver surgery and enabled increasing numbers of patients to undergo major hepatectomy. In addition, recent studies have suggested that age did not appear to be a risk factor influencing short- or

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Table 1 Comparison of clinical characteristics between the young and elderly groups

	Total *N* (%) *N* = 93	Young (<70 years) *n* (%) *n* = 62	Elderly (≥70 years) *n* (%) *n* = 31	*P*
Age, median, range (year)	64 (32–85)	59 (32–69)	75 (70–85)	<0.0001
Male gender	57 (61.3)	36 (58.1)	21 (67.7)	0.498
ASA grade I/II/III	18/54/21	13/38/11	5/16/10	0.284
BMI, median (range)	25.0 (15.9–35.5)	24.6 (15.9–35.5)	25.6 (20.3–33.1)	0.026
Alcohol	15 (16.1)	8 (12.9)	7 (22.6)	0.245
Smoking	17 (18.3)	10 (16.1)	7 (22.6)	0.570
Comorbidity				
Diabetes mellitus	7 (7.5)	3 (4.8)	4 (12.9)	0.216
Hypertension	24 (25.8)	11 (17.7)	13 (41.9)	0.022
Hyperlipidemia	18 (19.4)	11 (17.7)	7 (22.6)	0.587
Ischemic heart disease	11 (11.8)	6 (9.7)	5 (16.1)	0.496
COPD	9 (9.7)	5 (8.1)	4 (12.9)	0.474
Viral status				
HBV	0 (4)	0 (4)	0 (4)	–
HCV	1 (1.1)	1 (1.6)	0 (4)	1.000
Charlson Comorbidity Index, median (range)	3 (2–8)	2 (2–7)	3 (2–8)	0.113
Comorbidities ≥2	17 (18.3)	7 (11.3)	10 (32.3)	0.021
Diagnosis				
Colon cancer metastases	65 (69.9)	38 (61.3)	27 (87.1)	0.015
Rectal cancer metastases	28 (30.1)	24 (38.7)	4 (12.9)	0.015
Previous abdominal operation	80 (86.0)	53 (85.5)	27 (87.1)	1.000
Previous hepatectomy	26 (28.0)	16 (25.8)	10 (32.3)	0.624
Preoperative chemotherapy	65 (69.9)	47 (75.8)	18 (58.1)	0.096
Preoperative PVE	17 (18.3)	13 (21.0)	4 (12.9)	0.406
Median tumor size (range)	35 (7–140)	35 (7–140)	34 (10–100)	0.483
Tumor size ≥5 cm	28 (30.1)	18 (29.0)	10 (32.3)	0.812
Tumor number, median (range)	2.0 (1–8)	2.0 (1–6)	2.0 (1–8)	0.512
Right hepatectomy	62 (66.7)	42 (67.7)	20 (64.5)	0.817
Left hepatectomy	12 (12.9)	7 (11.3)	5 (16.1)	0.525
Right trisectionectomy	9 (9.7)	6 (9.7)	3 (9.7)	1.000
Left trisectionectomy	6 (6.5)	5 (8.1)	1 (3.2)	0.659
Central hepatectomy	4 (4.3)	2 (3.2)	2 (6.5)	0.598
Right-sided hepatectomy (right hepatectomy + right trisectionectomy)	71 (76.3)	48 (77.4)	23 (74.2)	0.797
Left-sided hepatectomy (left hepatectomy + left trisectionectomy)	18 (19.4)	12 (19.4)	6 (19.3)	0.781
Simultaneous intrahepatic procedure				
Wedge resection	28 (30.1)	21 (33.9)	7 (22.6)	0.340
Radiofrequency ablation	14 (15.1)	7 (11.3)	7 (22.6)	0.217
Combined resection of adjacent organs	5 (5.4)	2 (3.2)	3 (9.7)	0.328
Diaphragm	3 (3.2)	1 (1.6)	2 (6.5)	0.256
Common bile duct	1 (1.1)	1 (1.6)	0 (4)	1.000
Duodenum	1 (1.1)	0 (4)	1 (3.2)	0.333
Surgical duration, min, median (range)	274 (100–540)	300 (100–540)	240 (135–515)	0.920
Use of Pringle maneuver	12 (12.9)	9 (14.5)	3 (9.7)	0.744
Blood loss, mL, median (range)	300 (10–3000)	400 (10–3000)	300 (50–1500)	0.361
Intraoperative transfusion	10 (10.8)	6 (9.7)	4 (12.9)	0.726

Table 1 continued

	Total *N* (%) $N = 93$	Young (<70 years) *n* (%) $n = 62$	Elderly (≥70 years) *n* (%) $n = 31$	*P*
Conversion	10 (10.8)	6 (9.7)	4 (12.9)	0.726
Drain	22 (23.7)	18 (29.0)	4 (12.9)	0.120
R0 resection	85 (91.4)	59 (95.2)	26 (83.9)	0.116

ASA American Society of Anesthesiologists physical status classification, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *HCC* hepatocellular carcinoma, *PVE* portal vein embolization

long-term outcomes after resection of CRLM [4–10]. In light of these findings, elderly patients with CRLM are increasingly being considered for treatment strategies similar to those of their younger counterparts.

Laparoscopic liver resection has greatly evolved during the past several years [11–17]. Several reports indicated that laparoscopic hepatectomy is associated with less blood loss, lower use of narcotics, and shorter hospital stay, with no difference in complication rates or oncological outcomes compared with open hepatectomy [18–20]. However, to date, there exists very limited evidence on the outcome after laparoscopic major hepatectomy (LMH) in elderly patients. Therefore, the objective of this retrospective study was to assess the influence of age on postoperative outcomes after LMH.

Materials and methods

Study population

Data of all consecutive patients who underwent LMH for CRLM at Institut Mutualiste Montsouris (Paris, France) from January 1998 to September 2013 were retrieved from a prospective database for this retrospective study. Major hepatectomy was defined as the resection of ≥3 contiguous segments, according to Couinaud's classification [21]. Patients with an incomplete work-up or insufficient follow-up (<6 months) were excluded from analysis, and those that met the inclusion criteria were divided into two age groups: ≥70 years (elderly group, $n = 31$) and <70 years (young group $n = 62$).

For comparisons, the 31 elderly patients undergoing LMH were individually matched to two control patients according to demographics, tumor characteristics, and details of surgical procedures based on the following criteria: gender, American Society of Anesthesiologists score, chemotherapy before surgery, location (anterior vs. posterior; deep vs. superficial), maximum diameter, and number of lesions, portal vein embolization (PVE), and extent of hepatectomy. A waiver of authorization was obtained from the Institutional Review Board of the Institut Mutualiste Montsouris to conduct this study.

Preoperative evaluation

Preoperative investigations included complete blood and liver function tests as well as routine cardiorespiratory evaluation. Computed tomography and magnetic resonance imaging during the later years of the study were performed to assess both underlying liver and tumor characteristics. Preoperative percutaneous biopsy of the nontumorous parenchyma and PVE were performed on a case-by-case basis [22]. Surgical risk was assessed using the criteria of the American Association of Anesthesiologists (ASA) and Charlson comorbidity index (CCI) according to clinical data. CCI was used to predict the risk of death from comorbid disease using weighted scores for the following comorbidities: coronary artery disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, hemiplegia, chronic renal disease, cancer, metastases, and acquired immunodeficiency syndrome [23]. In the present study, CCI was based on all comorbidities recorded at the inclusion visit. Pulmonary comorbidity was defined as chronic and severe limitation of mobility (obstructive, restrictive, and vascular) and inability to perform household chores, whereas cardiovascular comorbidity was defined as symptomatic coronary heart disease with New York Heart Association stage 2 and 3 clinical limitations or myocardial infarction during the previous 6 months. Acute kidney injury was defined as an absolute increase in serum creatinine of ≥0.3 mg/dL (≥26.4 μm/L) or ≥50 % increase in serum creatinine and reduction in urine output of <0.5 mL/kg/h for more than 6 h over a time period of <48 h. Chronic kidney disease was defined as either kidney damage or a decreased glomerular filtration rate of less than 60 mL/min/1.73 m^2 for ≥3 months.

Table 2 Comparisons between postoperative outcomes between the young and elderly groups

	Total *N* (%) *N* = 93 (100.0)	Young (<70 years) *n* (%) *n* = 62 (66.7)	Elderly (≥70 years) *n* (%) *n* = 31 (33.3)	*P*
Postoperative mortality	0 (4)	0 (4)	0 (4)	–
Postoperative complication	47 (50.5)	34 (54.8)	13 (41.9)	0.276
Liver-specific complication	27 (29.0)	21 (33.9)	6 (19.4)	0.225
Biliary leakage	10 (10.8)	9 (14.5)	1 (3.2)	0.156
Liver failure	11 (11.8)	8 (12.9)	3 (9.7)	0.746
Ascites	3 (3.2)	2 (3.2)	1 (3.2)	1.000
Intra-abdominal abscess	3 (3.2)	2 (3.2)	1 (3.2)	1.000
General complication	20 (21.5)	13 (21.0)	7 (22.6)	1.000
Fever	4 (4.3)	4 (6.5)	0 (4)	0.297
Leukocytosis	1 (1.1)	1 (1.6)	0 (4)	1.000
Pleural effusion	6 (6.5)	2 (3.2)	4 (12.9)	0.092
Other pulmonary	2 (2.2)	0 (4)	2 (6.5)	0.108
Parietal	1 (1.1)	1 (1.6)	0 (4)	1.000
Others	6 (6.5)	5 (8.1)	1 (3.2)	0.659
Postoperative major complication	22 (23.7)	17 (27.4)	5 (16.1)	0.303
Biliary leakage	9 (9.7)	8 (12.9)	1 (3.2)	0.263
Liver failure	2 (2.2)	2 (3.2)	0 (4)	0.550
Ascites	2 (2.2)	1 (1.6)	1 (3.2)	1.000
Intra-abdominal abscess	3 (3.2)	2 (3.2)	1 (3.2)	1.000
Pleural effusion	1 (1.1)	1 (1.6)	0 (4)	1.000
Ileus	3 (3.2)	1 (1.6)	2 (6.5)	0.256
Septic shock	1 (1.1)	1 (1.6)	0 (4)	1.000
Parietal	1 (1.1)	1 (1.6)	0 (4)	1.000
Reoperation	2 (2.2)	1 (1.6)	1 (3.2)	1.000
Length of hospital stay, days (range)	10.0 (5–57)	11.0 (5–57)	8.5 (5–44)	0.501

Surgical procedures

All resections were performed with curative intent. The surgical procedure, including trocar placement, has been described elsewhere [11–15, 24]. All intraoperative parameters, including type and duration of vascular clamping, blood loss with subsequent blood transfusion, and duration of surgery, were recorded.

Postoperative outcomes

Postoperative complications were stratified according to the Clavien–Dindo classification [25], which defines major complications by a score of ≥3. If the patient had two or more complications, the most severe was selected for analysis. Specific liver complications often encountered after major liver procedures included the following: liver failure according to the "50–50 criteria" on postoperative day 5 [26]; ascites, defined as an abdominal drainage output of more than 10 mL/kg body weight/day after postoperative day 3 [27]; and biliary leakage, defined by a bilirubin concentration in the drainage fluid of more than three-fold of that in the serum [28]. Both complications and postoperative mortality were considered as those occurring within 90 days of the surgery or at any time during the postoperative hospital stay. Pathological resection margin was classified as R0 (microscopically >1 mm from the resection margin) or R1 (microscopically <1 mm from the resection margin).

Statistical analysis

Patient baseline characteristics are expressed as medians for continuous data and numbers with percentages for categorical data. Preoperative, intraoperative, and postoperative characteristics, as well as long-term patient survival, were compared between the age groups (elderly vs. young). Fisher's exact test was used to identify differences in categorical variables and the Wilcoxon rank-sum test for continuous variables. Overall survival was defined as time from surgery to death (all causes). Cumulative overall survival rates were determined using the Kaplan–Meier method and compared using the log-rank test. All tests were two-sided. A probability (*P*) value <0.05 was

Table 3 Comparisons of long-term outcomes between the young and elderly groups

	Total *N* (%) *N* = 93 (100.0)	Young (<70 years) *n* (%) *n* = 62 (66.7)	Elderly (≥70 years) *n* (%) *n* = 31 (33.3)	*P*
Recurrence	63 (67.7)	44 (71.0)	19 (61.3)	0.357
None	30 (32.3)	18 (29.0)	12 (38.7)	0.357
Liver	27 (29.0)	19 (30.6)	8 (25.8)	0.809
Extrahepatic	17 (18.3)	11 (17.7)	6 (19.4)	1.000
Both	19 (20.4)	14 (22.6)	5 (16.1)	0.589
Last follow-up				
Alive	50 (53.8)	34 (54.8)	16 (51.6)	0.827
Dead	43 (46.2)	28 (45.2)	15 (48.4)	
Alive without disease	34 (36.6)	23 (37.1)	11 (35.5)	1.000
Alive with disease	16 (17.2)	11 (17.7)	5 (16.1)	
Died from disease	38 (40.9)	25 (40.3)	13 (41.9)	1.000
Died from other cause	5 (5.4)	3 (4.8)	2 (6.5)	

considered statistically significant. Statistical analyses were performed using SPSS® version 20.0 for Windows® software (IBM Corporation, Armonk, NY, USA).

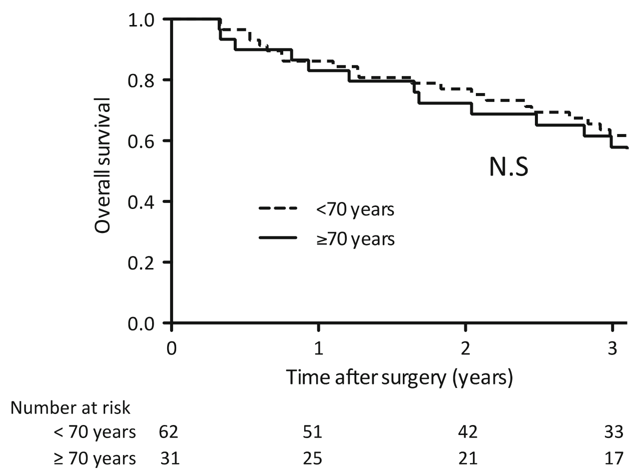
Results

Preoperative characteristics

Clinical characteristics are detailed in Table 1. There were 31 and 62 patients in the elderly and young groups, respectively. The groups were well matched for gender, ASA grade, body mass index, viral status, and CCI. However, the elderly group included patients characterized by more hypertension (41.9 vs. 17.7 %, $P = 0.022$). Moreover, the proportion of patients with two or more comorbidities was significantly higher in the elderly group ($n = 10$, 32.3 %) than in the young group ($n = 7$, 11.3 %; $P = 0.021$).

Rectal cancer metastases were less common in the elderly group compared with the young group (12.9 vs. 38.7 %, $P = 0.015$). There was no difference in the proportion of patients who underwent previous abdominal surgery or hepatectomy, or received preoperative chemotherapy or PVE between the groups. The proportion of patients with a maximum tumor diameter of ≥5 cm was 32.3 % ($n = 10$) in the elderly group and 29.0 % ($n = 18$) in the young group ($P = 0.812$). There were no significant differences in maximum tumor diameter and tumor number between the groups.

There was no significant difference in extent of resection, contralateral wedge resection, or combined resections of adjacent organs between the elderly and young groups, whereas surgical duration was comparable (300 min in the



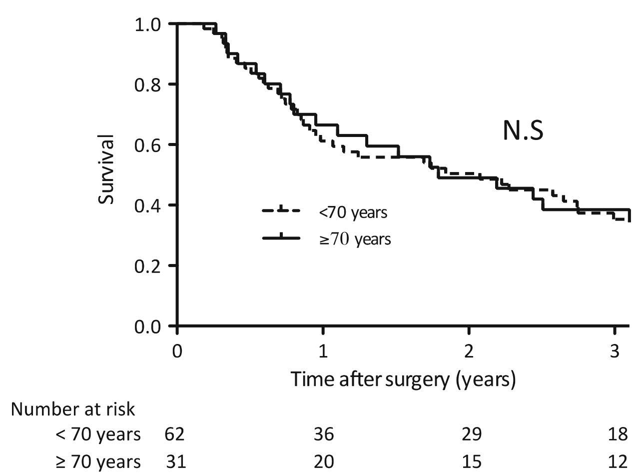


Fig. 1 (*Upper*) Overall survival for all patients in the elderly and young groups. $P = 0.842$ (log-rank test) (*Lower*) Disease-free survival of patients in the elderly and young groups. $P = 0.676$ (log-rank test)

Table 4 Reported series on major liver resection for colorectal liver metastases in the elderly

First author	Year	Age cut-off	*N*	Major resection %	Mortality %	Overall morbidity %	Overall survival %	Disease-free survival %
Nagano et al. [4]	2005	71	62	32.8	0	19.7	46.5 (3-year) 34.1 (5-year)	50.7 (5-year)
Mazzoni et al. [5]	2007	70	53	32.0	5.7	20.7	30.0 (5-year)	–
Adam et al. [6]	2010	70	1624	47.7	3.8	32.3	57.1 (3-year)	37.0 (3-year)
Di Benedetto et al. [7]	2011	70	32	59.4	3.0	28.1	51.9 (3-year) 33.3 (5-year)	29.2 (3-year) 19.5 (5-year)
Cannon et al. [8]	2011	70	59	52.5	0	52.5	47.6 (3-year) 20.9 (5-year)	22.3 (3-year) 16.7 (5-year)
Kulik et al. [9]	2011	70	190	43.8	0.5	12.3	31.8 (5-year)	–
Cook et al. [10]	2012	75	151	54.3	7.3	32.5	37.0 (5-year)	–
Present series	2014	70	31	100	0	54.8	57.9 (3-year)	38.5 (3-year)

young group vs. 240 min in the elderly group, $P = 0.920$). There were no significant differences in blood loss, vascular clamping, intraoperative transfusion, and conversion. In addition, there was no notable difference in the incidence of R0 resection between the groups.

Perioperative mortality and postoperative complications

No patient died within 90 days after the hepatectomy (Table 2). Postoperative morbidity occurred in 41.9 % of patients aged ≥70 years and in 54.8 % of the young patients ($P = 0.276$). The morbidity rates were 47.8 % (11/23) and 58.3 % (28/48) after right-sided major hepatectomy (P = 0.452), and 33.3 % (2/6) and 33.3 % per (4/12) after left-sided major resection ($P = 1.000$) in the elderly and young patients, respectively. The postoperative morbidity rate was 37.5 % for patients aged 70–75 years ($n = 16$) and 46.7 % for those aged 76–85 ($n = 15$) years ($P = 0.722$). No significant difference in morbidity was observed between patients who did or did not receive preoperative chemotherapy (50 vs. 50.7 %, $P = 1.000$). The median hospital stay of all patients was 10 days (range 5–57 days) with no observed difference between the elderly and young groups (8.5 vs. 11.0 days, respectively; $P = 0.501$).

Tumor recurrence and survival

Patients with insufficient follow-up (<6 months) were excluded in the present study. Among them, no patient died within 6 months after operation. After a median follow-up period of 39 (range 3–84) months for the entire study population, 61.3 % of the patients developed tumor recurrence in the elderly group compared with 71.0 % in the young group ($P = 0.357$) (Table 3). The 3-year overall survival rate was 57.9 % in the elderly group (median survival 39 months) and 61.7 % in the young group (median survival 40 months) ($P = 0.842$) (Fig. 1). A 3-year disease-free survival rate of 38.5 % was achieved in patients aged ≥70 years, which was not significantly different from that in the young patients (35.3 %; $P = 0.676$) (Fig. 1).

Discussion

The progress of LMH has been very slow worldwide because of its technical difficulties, fear of hemorrhage, and suspicion of oncological inadequacy; however, LMH has been increasingly reported by several high-volume academic centers [11–15, 29, 30]. To the best of our knowledge, this is the first single-center, case-matched study to evaluate treatment outcome of elderly patients undergoing LMH for CRLM. With some exceptions, most recent publications did not exclusively analyze LMH for CRLM [31, 32], but rather delivered only limited conclusions on the feasibility and safety of resection for CRLM in elderly patients. The results of the present series clearly suggest that LMH for CRLM in elderly patients is safe and does not contribute to higher rates of postoperative morbidity or mortality. Our results showed a lower mortality rate compared with those of previous series of open major hepatectomy [31, 32]. However, as shown in Table 1, a significant portion of elderly patients had comorbidities, including 16 % with ischemic heart disease and nearly 13 % with chronic obstructive pulmonary disease, in accordance with recent data published elsewhere [33–35]. Even though more than 30 % of the elderly patients were classified as ASA grade III and had more than two comorbidities, the present series confirms that postoperative overall complication and major complication rates were similar between young and elderly patients. We did not observe any difference in postoperative liver failure (12.9 vs. 9.7 %, respectively; $P = 0.746$). This result was similar in elderly patients who received >6 cycles of chemotherapy (46.8 vs. 48.4 %, $P = 1.000$) or who underwent preoperative PVE (21.0 vs. 12.9 %, $P = 0.406$).

Open major hepatectomies are mostly performed through bilateral subcostal or J-shaped incisions, with transection of the abdominal muscles with prolonged retraction of the right hemi-diaphragm. First, these large incisions may increase the risk of cardiopulmonary complications through several mechanisms, such as painful limitation of the thoracic cage excursion but also modification of diaphragmatic lymphatic vessel function following dissection in the vicinity of the diaphragm and the diaphragmatic peritoneum. This surgical aggression may result in a 50–60 % reduction of the vital capacity and a 30 % reduction in functional residual capacity [36]. On the opposite, the laparoscopic approach resulted in dramatically decreased surgical wall trauma since only 5 or 6 port incisions are performed, and the resected specimen is extracted through limited incisions including suprapubic incision without muscle section. In this context, decreased postoperative pain and early postoperative rehabilitation [37] may therefore provide improved cardiopulmonary function recovery. Furthermore, we observed non-significant trends toward higher rate of pulmonary complications in elderly patients even though the median operative time of LMH in these patients was relatively short (240 min), reducing the potential damage to the cardiopulmonary system.

Regarding long-term outcomes, our data showed no difference in overall survival between the groups. In most studies, the 3- and 5-year overall survival rates in patients ≥70 years of age were 46–57 and 20–37 %, respectively (Table 4). Long-term survival of elderly patients was slightly less than that of young patients, but still considerably long and acceptable [4, 6–8]. A large multicenter study, which included 7,764 patients undergoing open hepatectomy, found a significant difference in 3-year overall survival rates between young and elderly patients (60.2 vs. 57.1 %, respectively) [6]. The authors suggested that this difference might be due to more limited survival expectancy of the elderly patients and higher prevalence of comorbidity. The present series confirms this finding even though the limited sample size may explain the absence of statistical difference in overall and disease-free survivals.

The major limitations to the present study were the relatively small sample size and the retrospective nature of the analysis despite a prospective recording. Nevertheless, it represents the largest collection reported to date and we opted for a case-matched, control study design to decrease inherent bias.

In conclusion, LMH for CRLM in elderly patients is feasible and results in acceptable perioperative complications and long-term outcomes that are similar to those in young patients at high-volume laparoscopic liver centers, suggesting that advanced age itself should not be regarded as a contraindication for LMH.

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