JBUON 2017; 22(5): 1180-1185
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Safety and efficacy of liver resections in elderly patients

Georgios C. Sotiropoulos*, Ioannis D. Kostakis*, Nikolaos Machairas, Stylianos Kykalos, Gregory Kouraklis

Second Department of Propedeutic Surgery, "Laiko" General Hospital, National and Kapodistrian University of Athens, Medical School, Athens, Greece

*These authors contributed equally to this work and should be considered as co-first authors

Summary

Purpose: *Elderly patients constitute a special group of surgical candidates due to the frequent coexistence of major comorbidities. We report our experience in performing liver resections in patients aged 75 years or older.*

Methods: *During a period of 62 months, 154 patients underwent liver resections, out of which 20 were 75 years old or older. Our prospectively maintained database was reviewed regarding patient and tumor characteristics, intraoperative and postoperative data.*

Results: *Out of the 20 patients aged 75 years or older, 15 were men and 5 women, with a mean age of 79.3 years. Sixteen patients (80%) had at least one major comorbidity. Indications for surgery was hepatocellular carcinoma (n=5), intrahepatic cholangiocarcinoma (n=7), liver metastases (n=5), liver abscess (n=2) and liver cyst with hemorrhage (n=1). Liver resections included 3 left hepatectomies, 1 left lateral hepatectomy combined with segmentectomy and wedge resection, 2 right hepatectomies, 1 central hepatectomy, 4 bisegmentectomies, 3 segmentectomies, 4 wedge resections and 2 unroofings of giant liver cysts. In 10 out of the 20 operations, patients underwent further procedures apart from the liver resection. Six patients were postoperatively admitted to intensive care unit for 1 or 2 days. Postoperative bile leak was documented in 2 patients and postoperative hemorrhage in 1 patient, for which no reoperation was needed. No postoperative death was recorded during the hospitalization of the patients. The mean length of hospital stay was 12.9 days.*

Conclusions: *Liver resections, even major ones, can be tolerated by elderly patients with good postoperative outcomes under the presupposition of careful patient selection.*

Key words: *elderly, geriatric, hepatectomy, liver resection, older*

Introduction

Liver resection is the optimal therapeutic option for a variety of benign and malignant liver pathologies. Nevertheless, several complications have been related to hepatobiliary surgery, especially when it concerns major hepatectomies. The presence of major comorbidities has been associated with an increase in postoperative morbidity and mortality in this kind of procedures [1]. Elderly patients constitute a particular group of surgical candidates, as far as major operations are concerned. The decreased reserves of their cardiac, renal, pulmonary and hepatic function, along with the more frequent presence of comorbidities, when compared with younger patients, increase their susceptibility to postoperative complications. Therefore, surgeons were very skeptical and reluctant to subject elderly patients to hepatectomy in the past. However, several attempts to perform liver resections, and even major hepatectomies, in elderly patients have been reported in the literature, with acceptable rates of morbidity and mortality in carefully selected cases [2]. Herein, we report our experience in performing liver resections in patients aged 75 years old or older.

Correspondence to: Ioannis D. Kostakis, MD, MSc, PhD. Second Department of Propedeutic Surgery, "Laiko" General Hospital, National and Kapodistrian University of Athens, Medical School, 17 Agiou Thoma Street, 11527, Athens, Greece.
Tel: +30 6974906246, +30 2107709948, Fax: +30 2107709949, E-mail: i.d.kostakis@gmail.com
Received: 25/02/2017; Accepted: 10/03/2017

Methods

During a period of 62 months, between October 2011 and December 2016, 154 patients underwent liver resections by one senior hepatobiliary surgeon in our department for a variety of liver pathologies. Twenty out of the 154 patients were 75 years or older. Our prospectively maintained database was reviewed regarding patient and tumor characteristics, intraoperative and postoperative data. Patient characteristics included age, gender, body mass index (BMI), comorbidities, the American Society of Anesthesiologists (ASA) score [3], the Charlson comorbidity index [4] and whether there was any preoperative treatment or not. Tumor characteristics included diagnosis, whether the hepatic lesions were primary or metastatic and solid or cystic, the number and size of lesions, tumor location, the results of the imaging studies and the classification of tumor grade and stage following the 7th edition of the TNM Classification of Malignant Tumors according to the Union Internationale Contre le Cancer (UICC). Intraoperative data referred to the exact type of hepatic resection, any additional surgical procedures, duration of vascular occlusion (Pringle maneuver or total vascular occlusion), blood transfusion and total operating time. Postoperative data referred to whether there was direct postoperative extubation or not, whether patients were admitted to the intensive care unit (ICU) and for how long, the postoperative morbidity and 30-day mortality, the Dindo – Clavien classification of surgical complications [5] and the length of hospital stay. This study conformed to the ethical standards of the Ethics Committee of our institution and with the Declaration of Helsinki of 1975, as revised in 2000.

Results

Patient characteristics

Out of the 20 patients aged 75 years or older, 15 were men and 5 women. The mean age was 79.3±3.7 years and the median 78 years (min-max: 75-89 years). The mean BMI of our study population was 28.4±2.1 and the median was 28 (min-max: 25.6-31.8). As far as comorbidities are concerned, 16 patients (80%) had at least one major comorbidity. In particular, 3 patients had chronic hepatitis B infection, 12 suffered from arterial hypertension, 5 from diabetes mellitus type 2, 3 from atrial fibrillation and 3 from coronary disease, 2 had valvular heart disease, 1 had chronic obstructive pulmonary disease, 1 suffered from chronic lymphocytic leukemia and 2 were obese. Two patients also had synchronous colon cancer and 1 had previously resected rectal cancer, while 1 had synchronous gastric cancer and 1 had synchronous unresectable pancreatic cancer. Four patients had no major comorbidity. Twelve patients were classified to ASA score II and 8 to ASA score III. The mean Charlson comorbidity index was 5.8±2.4 and the median was 6 (min-max: 0-8). Concerning pretreatment, 3 patients had been subjected to preoperative chemoembolization for hepatocellular carcinoma. Patient characteristics are listed in Table 1. Our study conformed to the Declaration of Helsinki and was in accordance with the ethical standards of our institution.

Table 1. Patient characteristics

Characteristics	
Gender, n	
Male	15
Female	5
Age, years	
Mean ± SD	79.3±3.7
Median (min-max)	78 (75-89)
Body mass index	
Mean ± SD	28.4 ± 2.1
Median (min-max)	28 (25.6-31.8)
Comorbidities, n	
Chronic hepatitis B	3
Arterial hypertension	12
Diabetes mellitus type 2	5
Atrial fibrillation	3
Coronary disease	3
Valvular heart disease	2
Chronic obstructive pulmonary disease	1
Chronic lymphocytic leukemia	1
Obesity	2
Colorectal cancer	3
Gastric cancer	1
Pancreatic cancer	1
No major comorbidity	4
ASA score, n	
II	12
III	8
Charlson comorbidity index, n	
Mean ± SD	5.8±2.4
Median (min-max)	6 (0-8)

ASA: American Society of Anesthesiologists, SD: standard deviation

Tumor characteristics

There was a plethora of underlying liver pathologies in our study population. Five patients had hepatocellular carcinoma, 7 intrahepatic cholangiocarcinoma, 5 liver metastases (2 from colon cancer, 1 from rectal cancer, 1 from gastric cancer and 1 from pancreatic cancer), 2 liver abscess and 1 had a liver cyst with hemorrhage. Sixteen patients (80%) had a single liver lesion, whereas 4 patients (20%) had 2 or more liver lesions. Seventeen patients (85%) had unilobar disease (7 confined to the left hemiliver and 10 confined to the right hemiliver), whereas 3 patients (15%) had bilobar disease. The mean maximum diameter of

hepatic lesions was 6.6±5 cm and the median was 5.8 cm (min-max:1.2-21). The 5 cases of hepatocellular carcinoma corresponded to 1 pT1 tumor, 1 pT2 tumor, 2 pT3a tumors and 1 pT3b tumor, concerning the pT stage, and 4 grade II tumors and 1 grade III tumor, concerning the histologic grade. The 7 cases of intrahepatic cholangiocarcinoma corresponded to 3 pT1 tumors, 1 pT2a tumor, 1 pT2b tumor and 2 pT3 tumors, regarding the pT stage, and 1 grade I tumor, 4 grade II tumors and 2 grade III tumors, regarding the histologic grade. Tumor characteristics are listed in Table 2.

Table 2. Tumor characteristics

Characteristics	
Liver pathology, n	
Hepatocellular carcinoma	5
Intrahepatic cholangiocarcinoma	7
Liver metastases	5
Liver abscess	2
Liver cyst	1
Number of lesions, n	
Single lesion	16
Multiple lesions	4
Disease distribution, n	
Unilobar disease	17
Bilobar disease	3
Maximum tumor diameter, cm	
Mean ± SD	6.6±5
Median (min-max)	5.8 (1.2-21)
Hepatocellular carcinomas, n	
pT1	1
pT2	1
pT3a	2
pT3b	1
Grade II	4
Grade III	1
Intrahepatic cholangiocarcinomas, n	
pT1	3
pT2	1
pT3a	1
pT3b	2
Grade I	1
Grade II	4
Grade III	2

Intraoperative data

Liver resections included 3 left hepatectomies, 1 left lateral hepatectomy combined with segmentectomy and wedge resection, 2 right hepatectomies, 1 central hepatectomy, 4 bisegmentectomies (1 combined with radiofrequency ablation), 3 segmentectomies (2 performed laparoscopically), 4 wedge resections (1 performed laparoscopically) and 2 cases of laparoscopic unroofing of giant liver cysts (10cm and 21cm respectively). In 10 out of the 20 operations, patients underwent additional procedures apart from the liver resection. In particular, patients were subjected to additional cholecystectomy in 6 cases, right hemicolectomy in 2 cases, distal gastrectomy in 1 case and gastroenteric anastomosis, enterobiliary anastomosis and cholecystectomy (for unresectable pancreatic cancer) in 1 case.

Pringle maneuver for vascular occlusion was performed in 10 cases [mean duration±SD: 26.8±9.6, median (min-max): 25 min (15-45)], whereas total vascular occlusion was needed in 1 case for 8 min. The mean total operating time was 196.5±69.4 and the median was 180 min (min-max: 90-300). Intraoperative blood transfusion was needed in 14 cases. The mean amount of transfused blood units was 1.6±1.2 blood units and the median amount of transfused blood units was 2 blood units (min-max: 0-4). Intraoperative data are summarized in Table 3.

Table 3. Intraoperative data

Data	
Types of liver resection, n	
Left hepatectomy	3
Left lateral hepatectomy + segmentectomy + wedge resection	1
Right hepatectomy	2
Central hepatectomy	1
Bisegmentectomy	4 (1 combined with radiofrequency ablation)
Segmentectomy	3 (2 performed laparoscopically)
Wedge resection	4 (1 performed laparoscopically)
Laparoscopic liver cyst unroofing	2
Additional procedures (in 10 out of 20 operations), n	
Cholecystectomy	6
Right hemicolectomy	2
Distal gastrectomy	1
Gastroenteric anastomosis + enterobiliary anastomosis + cholecystectomy	1
Duration of Pringle maneuver (in 10 out of 20 operations)	
Mean ± SD	26.8±9.6
Median (min-max)	25 (15-45)
Total operating time, min	
Mean ± SD	196.5±69.4
Median (min-max)	180 (90-300)
Intraoperative blood transfusion, n	
Yes	14
No	6
Amount of intraoperatively transfused blood units, n	
Mean ± SD	1.6 blood units ± 1.2
Median (min-max)	2 blood units (0-4)

Postoperative data

Eighteen out of the 20 patients were directly extubated after the operation. Six patients were postoperatively admitted to ICU for 1 or 2 days for close monitoring, 2 who were transferred to ICU were intubated and 4 were extubated. Postoperative bile leak was documented in 2 patients, which was treated with endoscopic retrograde cholangiopancreatography (ERCP) and placement of an extrahepatic bile duct stent in one patient who had undergone right hepatectomy and cholecystectomy, and with ERCP and percutaneous drainage of biloma in the other case, following a caudate lobectomy (segment I). Postoperative hemorrhage was also documented in 1 patient after open bisegmentectomy, which was manifested with blood discharge from the drain and drop of hemoglobin levels. It was successfully treated conservatively with blood and plasma transfusions, administration of coagulation factors and close monitoring of vital signs, not requiring any additional intervention. No reoperation was needed in our study population and no postoperative death was recorded during the hospitalization of the patients. In regards to the Dindo-Clavien classification of surgical complications, 15 patients had grade I complications, 3 grade II complications and 2 grade IIIa complications. The mean length of hospital stay was 12.9±7.7 days and the median was 10 (min-max:7-40). Postoperative data are summarized in Table 4.

Table 4. Postoperative data

Data	
Direct extubation, n	
Yes	18
No	2
Admission to intensive care unit, n	
Yes	6
No	14
Postoperative complications, n	
Bile leak	2
Hemorrhage	1
Reoperation	0
Death	0
Dindo-Clavien classification of surgical complications, n	
Grade I	15
Grade II	3
Grade IIIa	2
Length of hospital stay, days	
Mean ± SD	12.9±7.7
Median (min-max)	10 (7-40)

Discussion

The specific group of elderly patients is characterized by the frequent coexistence of major comorbidities, which render their health fragile, and the decreased reserves in cardiac, renal, pulmonary and hepatic function, which are linked with the advanced age. The higher susceptibility of these patients to postoperative complications when compared with younger patients made surgeons reluctant to subject them to major operations in the past [6]. This is the reason why liver resections, and especially major hepatectomies, have been adopted with delay in older patients [2]. However, there is growing evidence that elderly patients can be subjected to major operations, such as colectomies and pancreatectomies, with acceptable rates of postoperative morbidity and mortality if there is careful patient selection [7,8].

Several attempts to study the efficacy and safety of hepatectomies in older patients have been published. There is no unanimous cut-off point for differentiating older from younger patients. However, most studies used 70 [9-19] or 75 years of age as a threshold [20-29]. All types of liver resections, from wedge resections or segmentectomies up to hemihepatectomies, have been performed in elderly patients. Even though there is a number of studies concluding that the rates of postoperative morbidity and/or mortality are higher in older patients who have undergone liver resection when compared with younger ones [13,14,18,20-23,26,27], there is also a considerable amount of studies suggesting that if older patients are considered fit to undergo a hepatectomy, there is no actual difference in postoperative outcomes between them and younger patients [9-12,24,25,28,30,31].

Even though many studies included patients with various underlying liver pathologies, there are several studies focusing on distinct liver pathologies, mostly on hepatocellular carcinoma [15,16,24,26,31-37] and colorectal metastases to the liver [14,25,27,28,38,39], and secondarily on other types, such as intrahepatic cholangiocarcinoma [18]. There is no unanimity among the various studies regarding postoperative outcomes when comparing older with younger patients for both hepatocellular carcinoma and colorectal metastases. Several studies on liver resections for hepatocellular carcinoma report that there is no actual difference between older and younger patients [32,35,37], but other studies suggest that the advanced age predisposes to higher rates of postoperative complications [33,34]. The same goes for liver resections for colorectal metastases, with

some studies supporting the disadvantage of advanced age [14,27], whereas others conclude that age does not affect postoperative outcomes significantly [25,28,39]. The one study comparing older and younger patients undergoing hepatectomy for intrahepatic cholangiocarcinoma concluded that postoperative mortality is similar between these two groups, but elderly patients are more likely to develop a major postoperative complication [18].

Apart from the advanced age, the existence of comorbidities and the exact type of them have also been evaluated as potential predictors of worse postoperative outcomes. The presence of comorbidities such as liver cirrhosis, chronic renal disease, chronic obstructive pulmonary disease, stroke, coronary disease, heart failure, atrial fibrillation, arterial hypertension and diabetes mellitus have been associated with higher postoperative rates of morbidity and/or mortality when compared with the presence of only minor comorbidities or the absence of any other disease [12,16,21,22]. Indicative of the contribution of major comorbidities to worse postoperative outcomes is the association between an ASA score of 3 or higher and increased rates of postoperative complications [13,21,22]. However, careful selection and individualized preparation for surgery of patients with high ASA score can reduce or prevent postoperative complications [40].

Our study population is a small group of elderly patients with a plethora of liver pathologies who were subjected in many types of liver resections, from wedge resection up to hemihepatectomy, which were combined in some cases with additional procedures. Even though most patients had at least one major comorbidity, the postoperative outcomes were remarkable. In particular, no postoperative death was recorded and the only major complications that were recorded, two cases of bile leak and one case of hemorrhage, were treated without reoperation and were well tolerated by the patients. These findings lead to the conclusion that liver resections, even major ones, can be tolerated by elderly patients with good postoperative outcomes provided careful patient selection will be carried out.

Conflict of interests

The authors declare no confict of interests.

References

1. Russell MC. Complications following hepatectomy. Surg Oncol Clin N Am 2015;24:73-96.
2. Phan K, An VV, Ha H, Phan S, Lam V, Pleass H. Hepatic resection for malignant liver tumours in the elderly: a systematic review and meta-analysis. ANZ J Surg 2015;85:815-22.
3. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. JAMA 1961;178:261-6.
4. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
5. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.
6. Knittel JG, Wildes TS. Preoperative assessment of geriatric patients. Anesthesiol Clin 2016;34:171-83.
7. Fontani A, Martellucci J, Civitelli S, Tanzini G. Outcome of surgical treatment of colorectal cancer in the elderly. Updates Surg 2011;63:233-7.
8. Casadei R, Taffurelli G, Silvestri S, Ricci C, Campra D, Minni F. Is age a barrier to pancreaticoduodenectomy? An Italian dual-institution study. Updates Surg 2015;67:439-47.
9. Hanazaki K, Kajikawa S, Shimozawa N et al. Hepatic resection for hepatocellular carcinoma in the elderly. J Am Coll Surg 2001;192:38-46.
10. Kondo K, Chijiiwa K, Funagayama M, Kai M, Otani K, Ohuchida J. Hepatic resection is justified for elderly patients with hepatocellular carcinoma. World J Surg 2008;32:2223-9.
11. Kaibori M, Matsui K, Ishizaki M et al. Hepatic resection for hepatocellular carcinoma in the elderly. J Surg Oncol 2009;99:154-60.
12. Hirokawa F, Hayashi M, Miyamoto Y et al. Surgical outcomes and clinical characteristics of elderly patients undergoing curative hepatectomy for hepatocellular carcinoma. J Gastrointest Surg 2013;17:1929-37.
13. Schiergens TS, Stielow C, Schreiber S et al. Liver resection in the elderly: significance of comorbidities and blood loss. J Gastrointest Surg 2014;18:1161-70.
14. Nachmany I, Pencovich N, Zohar N et al. Resection of colorectal liver metastases in the elderly-Is it justified? J Surg Oncol 2016;113:485-8.
15. Harimoto N, Yoshizumi T, Shimokawa M et al. Sarcopenia is a poor prognostic factor following hepatic resection in patients aged 70 years and older with hepatocellular carcinoma. Hepatol Res 2016;46:1247-55.
16. Kaibori M, Ishizaki M, Matsui K et al. Geriatric assessment as a predictor of postoperative complications in elderly patients with hepatocellular carcinoma. Lan-

genbecks Arch Surg 2016;401:205-14.

17. Andert A, Lodewick T, Ulmer TF et al. Liver resection in the elderly: A retrospective cohort study of 460 patients - Feasible and safe. Int J Surg 2016;28:126-30.
18. Vitale A, Spolverato G, Bagante F et al. A multi-institutional analysis of elderly patients undergoing a liver resection for intrahepatic cholangiocarcinoma. J Surg Oncol 2016;113:420-6.
19. Watanabe Y, Kuboki S, Shimizu H et al. A new proposal of criteria for the future remnant liver volume in older patients undergoing major hepatectomy for biliary tract cancer. Ann Surg 2016 Nov 15. [Epub ahead of print].
20. Sulpice L, Rayar M, Campillo B et al. Advanced age remains an achilles heel for liver resections. World J Surg 2014;38:918-26.
21. Reddy SK, Barbas AS, Turley RS et al. Major liver resection in elderly patients: a multi-institutional analysis. J Am Coll Surg 2011;212:787-95.
22. Tzeng CW, Cooper AB, Vauthey JN, Curley SA, Aloia TA. Predictors of morbidity and mortality after hepatectomy in elderly patients: analysis of 7621 NSQIP patients. HPB (Oxford) 2014;16:459-68.
23. Orcutt ST, Artinyan A, Li LT et al. Postoperative mortality and need for transitional care following liver resection for metastatic disease in elderly patients: a population-level analysis of 4026 patients. HPB (Oxford) 2012;14:863-70.
24. Motoyama H, Kobayashi A, Yokoyama T et al. Impact of advanced age on the short- and long-term outcomes in patients undergoing hepatectomy for hepatocellular carcinoma: a single-center analysis over a 20-year period. Am J Surg 2015;209:733-41.
25. Nardo B, Serafini S, Ruggiero M et al. Liver resection for metastases from colorectal cancer in very elderly patients: New surgical horizons. Int J Surg 2016;33:S135-41.
26. Cannistrà M, Grande R, Ruggiero M et al. Resection of hepatocellular carcinoma in elderly patients and the role of energy balance. Int J Surg 2016;33:S119-25.
27. Bell R, Pandanaboyana S, Nisar S et al. The impact of advancing age on recurrence and survival following major hepatectomy for colorectal liver metastases. J Gastrointest Surg 2017;21:266-74.
28. Gandy RC, Stavrakis T, Haghighi KS. Short- and long-term outcomes of elderly patients undergoing liver resection for colorectal liver metastasis. ANZ J Surg 2016 Oct 30. [Epub ahead of print].
29. Sgourakis G, Sotiropoulos GC, Bockhorn M et al. Liver resections for primary liver malignancies in the elderly. Acta Chir Belg 2009;109:340-4.
30. Portolani N, Baiocchi GL, Coniglio A et al. Limited liver resection: a good indication for the treatment of hepatocellular carcinoma in elderly patients. Jpn J Clin Oncol 2011;41:1358-65.
31. Hamaoka M, Kobayashi T, Ishiyama K et al. Evaluation of the risk factors and prognostic factors of hepatectomy for hepatocellular carcinoma in patients aged 80 years or more. J Hepatobiliary Pancreat Sci 2017;24:58-64.
32. Yamada S, Shimada M, Miyake H et al. Outcome of hepatectomy in super-elderly patients with hepatocellular carcinoma. Hepatol Res 2012;42:454-8.
33. Wang HQ, Yang J, Yan LN, Zhang XW, Yang JY. Liver resection in hepatitis B related-hepatocellular carcinoma: clinical outcomes and safety in elderly patients. World J Gastroenterol 2014;20:6620-25.
34. Nanashima A, Abo T, Nonaka T et al. Prognosis of patients with hepatocellular carcinoma after hepatic resection: are elderly patients suitable for surgery? J Surg Oncol 2011;104:284-91.
35. Kim JM, Cho BI, Kwon CH et al. Hepatectomy is a reasonable option for older patients with hepatocellular carcinoma. Am J Surg 2015;209:391-7.
36. Ueno M, Hayami S, Tani M, Kawai M, Hirono S, Yamaue H. Recent trends in hepatectomy for elderly patients with hepatocellular carcinoma. Surg Today 2014;44:1651-9.
37. Tsujita E, Utsunomiya T, Ohta M et al. Outcome of repeat hepatectomy in patients with hepatocellular carcinoma aged 75 years and older. Surgery 2010;147:696-703.
38. Schmidt T, Strowitzki MJ, Reissfelder C et al. Influence of age on resection of colorectal liver metastases. J Surg Oncol 2015;111:729-39.
39. Cannon RM, Martin RC, Callender GG, McMasters KM, Scoggins CR. Safety and efficacy of hepatectomy for colorectal metastases in the elderly. J Surg Oncol 2011;104:804-8.
40. Sotiropoulos GC, Machairas N, Stratigopoulou P, Kostakis ID, Mantas D, Kouraklis G. Laparoscopic liver resection for malignancy in high-risk surgical patients according to ASA classification. J BUON 2016;21:1398-1402.