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ORIGINAL ARTICLE

Impact of Liver Cirrhosis on Perioperative Outcomes Among Elderly Patients Undergoing Hepatectomy: the Effect of Minimally Invasive Surgery

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Abstract

Background The impact of cirrhosis on perioperative outcomes for elderly patients undergoing hepatectomy remains not well defined. We sought to determine the influence of underlying cirrhosis and minimally invasive surgery (MIS) on postoperative outcomes among elderly patients who underwent a hepatectomy.

Methods Patients who underwent hepatectomy between 2013 and 2015 were identified using the Center for Medicare Services (CMS) 100% Limited Data Set (LDS) Standard Analytic Files (SAFs). Short-term outcomes after hepatectomy, stratified by the presence of cirrhosis and MIS, were examined.

Results Among 7452 patients who underwent a hepatectomy, a minority had cirrhosis ($n = 481$, 6.5%) whereas the vast majority did not ($n = 6971$, 93.5%). Overall, median patient age was 72 years (IQR 68–76) and preoperative Charlson comorbidity score was 6 (IQR 2–8). Patients with cirrhosis were more likely to be younger (median age 71 [67–76] vs 72 [IQR 68–76] years), male (64.4% vs 50%), African American (8.1% vs 6.4%) and have a malignant diagnosis (87.1% vs 78.7%) compared to non-cirrhotic patients (all $p < 0.001$). There was no difference among patients with and without cirrhosis regarding type of hepatectomy or surgical approach (open vs MIS) (both $p > 0.05$). Patients with versus without cirrhosis had similar complication rates (24.1% vs 22.3%, $p = 0.36$), as well as 30-day (6.2% vs 5%, $p = 0.25$) and 90-day (10.4% vs 8.5%, $p = 0.15$) mortality. MIS reduced the length-of-stay in non-cirrhotic patients (OR 0.79, 95% CI 0.62–0.99, $p < 0.05$), yet was not associated with morbidity or mortality (both $p > 0.05$).

Conclusion The presence of cirrhosis did not generally impact outcomes in elderly patients undergoing hepatectomy for benign and malignant diseases. MIS hepatectomy in the elderly Medicare beneficiary population reduced LOS among patients without cirrhosis, yet was not associated with differences in morbidity or mortality.

Keywords Cirrhosis · Elderly · Hepatectomy · Outcomes

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Introduction

Liver disease is a major health problem in the USA.[1] According to the Centers for Disease Control and Prevention (CDC), chronic liver disease and cirrhosis are considered the 12th leading cause of death in the USA and are responsible for over 60,000 deaths annually.[2] Cirrhosis due to any cause predisposes to the development of hepatocellular carcinoma (HCC) with the majority of patients diagnosed with HCC worldwide having underlying cirrhosis.[3] In the USA, approximately 30,000 new patients are diagnosed with cirrhosis at tertiary referral centers each year.[4] Liver resection is associated with high morbidity and mortality, especially among patients with cirrhosis.[5–7] The higher morbidity and mortality may be due, in part, to difficult mobilization and transection of the fibrotic parenchyma, elevated portal pressure, impaired coagulation, and, in turn, higher risk of excessive bleeding particularly in cirrhotic patients requiring major operations.[8] Of note, an increase in life expectancy, especially in Western countries, has resulted in a higher proportion of elderly patients requiring surgery.[9] Elderly patients have more comorbidities, while age-associated changes can contribute to reduced hepatic regenerative capacity.[10] Owing to improvements in surgical techniques, anesthesia and medical care, cirrhosis is not considered an absolute contraindication for major surgery in elderly patients, although reports on morbidity and mortality remain inconsistent.[5,11–15]

The introduction of minimally invasive surgery (MIS), including laparoscopic (LH) and robotic surgery, has further enhanced outcomes among elderly patients undergoing bariatric, cholecystectomy, colectomy, hysterectomy, inguinal hernia, thoracic hernia, and ventral hernia procedures.[16,17] Indeed, laparoscopy can limit the amount of electrolytic and protein losses associated with open surgery[18] and, thus, be associated with lower morbidity, less bleeding, shorter operative time, and shorter length-of-stay (LOS).[19,20] In addition, robotic liver surgery has been suggested to be safe and efficient for both minor and major hepatic resections.[21]

The effects of cirrhosis on perioperative outcomes for older patients undergoing a hepatectomy still remain poorly defined.[8,19,20,22,23] Furthermore, the use of MIS for patients requiring hepatic resection in the presence of cirrhosis remains unknown. Although previous studies have investigated the impact of cirrhosis on outcomes following hepatic resection, there is a paucity of data regarding elderly patients with cirrhosis.[24] As such, the objective of the current study was to evaluate the impact of cirrhosis on postoperative outcomes after hepatectomy using a large national database. In addition, we sought to determine the effect of MIS on outcomes of interest among elderly patients undergoing hepatectomy.

Methods

Study Population and Data Collection

Patients 65 years of age or older who underwent a hemihepatectomy or partial hepatectomy for benign and malignant diseases between 2013 and 2015 were identified using the Center for Medicare Services (CMS) 100% Limited Data Set (LDS) Standard Analytic Files (SAFs) (Supplemental Table 1). Patients with additional non-hepatectomy procedures were excluded. Appropriate ICD-9 coding modifiers for laparoscopy and robotic surgery were used to identify people undergoing MIS. Patients who were enrolled in Medicare Part A and Part B, had no additional payments from a health maintenance organization (HMO), and had no record of payment made by a primary payer were selected.[1]

Patients with cirrhosis were identified based on the presence of ICD-9 CM codes prior to or at the time of surgery. Abstracted Medicare data included age, biologic sex, and clinical and perioperative information. Charlson comorbidity index score was computed using a validated algorithm.[25] Postoperative complications were determined using ICD-9 CM codes previously identified as having the highest sensitivity and specificity for identification of post-surgical complications.[26–28] Length-of-stay was calculated from the day of surgery to the day of discharge, with extended LOS defined as greater than the 75th percentile.[28]

Primary outcomes included incidence of perioperative complications within 30 and 90 days of surgical intervention. Secondary outcomes included the incidence of 30- and 90-day readmission and mortality, as well as LOS. Readmission was defined as admission to any hospital within 30 and 90 days of discharge. If a patient had more than one readmission, only the first readmission was evaluated.

Statistical Analysis

Categorical variables were presented as frequencies and percentages; continuous variables were presented as medians and interquartile ranges (IQR). Demographics, patient characteristics, and 30- and 90-day perioperative and postoperative outcomes including complications, LOS, and incidence of readmission and mortality were compared among patients with and without cirrhosis. Categorical variables were compared using chi-square tests and Fisher's exact tests where appropriate. Continuous variables were compared using the Wilcoxon rank-sum tests and the Kruskal-Wallis one-way analysis of variance.

Logistic regression was utilized to examine the relationship between MIS and outcomes of interest including incidence of a complication, extended LOS, discharge disposition other than home, 30- and 90-day readmission, and 30- and 90-day mortality. Additional analyses were performed to examine the

influence of the MIS approach on outcomes. Statistical significance was assessed at $\alpha = 0.05$. All analyses were performed using SAS v9.4.

Results

Patients Characteristics

Among 7452 patients who underwent a hepatectomy between 2013 and 2015, a minority had a concurrent diagnosis of cirrhosis ($n = 481$, 6.5%) whereas the vast majority did not have a history of cirrhosis ($n = 6971$, 93.5%). Overall, median patient age was 72 years (IQR 68–76) and preoperative Charlson comorbidity score was 6 (IQR 2–8). Approximately half of patients were male ($n = 3793$, 50.9%), and the majority were white ($N = 6541$, 87.8%). Most patients underwent a partial hepatectomy ($n = 5904$, 79.2%), while a smaller subset underwent a hemi-hepatectomy ($n = 1548$, 20.8%). Of note, malignancy was the most common indication for surgery (79.3% vs 20.7%, $p < 0.001$). Only a minority of patients ($n = 517$, 6.9%) underwent a minimally invasive hepatectomy.

Patients with cirrhosis were more likely to be younger (median age 71 [IQR 67–76] vs 72 [IQR 68–76] years, $p < 0.001$), male (64.4% vs 50%, $p < 0.001$), and African American (8.1% vs 6.4%, $p < 0.001$) and have a malignant diagnosis (87.1% vs 78.7%, $p < 0.001$) compared with non-cirrhotic patients. There was no difference among patients with versus without cirrhosis regarding type of hepatectomy performed (partial hepatectomy vs hemi-hepatectomy) or surgical approach (open vs MIS) (Table 1, both $p > 0.05$).

Perioperative Outcomes Following Hepatectomy

Approximately one in four patients ($n = 1671$, 22.4%) developed a complication during the index hospitalization. The most common complications were acute renal failure ($n = 899$, 12.1%), pulmonary failure ($n = 591$, 7.9%), and surgical site infection ($n = 525$, 7.0%) (Table 2). The median LOS for the index hospitalization was 6 (IQR 4–9) days. Roughly, 1 in 7 patients (15.7%) was readmitted within 30 days with one-fourth being readmitted within 90 days (25.1%); 30- and 90-day mortality was 5.1% and 8.6%, respectively. The incidence of perioperative 30- and 90-day complications related to pulmonary failure, pneumonia, myocardial infarction, DVT/PE, hemorrhage, surgical site infection, and GI hemorrhage was similar among patients with and without concurrent cirrhosis ($p > 0.05$). Specifically, the incidence of blood transfusion was similar between the two groups (cirrhosis 23.1% vs non-cirrhosis 19.5%, $p = 0.051$). Patients with cirrhosis did, however, have a higher incidence of acute renal failure within 30 days of discharge (4.2% vs 2.3%, $p = 0.013$). Among patients with and without cirrhosis, median LOS for the index admission was comparable (6 days (IQR 4, 8) vs 6 days (IQR 4, 9)), as was 30- and 90-day readmission and mortality irrespective of the presence of cirrhosis (all $p > 0.05$). In addition,

Table 1 Demographics and characteristics of patients who underwent hepatectomy stratified by presence of cirrhosis

Variable	Total $N = 7452$	No cirrhosis $N = 6971$	Cirrhosis $N = 481$	p
Age (median, IQR)	72 (68, 76)	72 (68, 76)	71 (67, 76)	< 0.001
Male	3793 (50.9%)	3483 (50%)	310 (64.4%)	< 0.001
Race				< 0.001
White	6541 (87.8%)	6153 (88.3%)	388 (80.7%)	
AA	485 (6.5%)	446 (6.4%)	39 (8.1%)	
Hispanic	33 (0.4%)	30 (0.4%)	3 (0.6%)	
Other/unknown	393 (5.3%)	342 (4.9%)	51 (10.6%)	
Charlson comorbidity index score (median, IQR)	6 (2, 8)	6 (2, 8)	5 (4, 8)	< 0.001
Indication				< 0.001
Benign	1544 (20.7%)	1482 (21.3%)	62 (12.9%)	
Malignancy	5908 (79.3%)	5489 (78.7%)	419 (87.1%)	
Procedure				0.82
Hemi-hepatectomy	1548 (20.8%)	1450 (20.8%)	98 (20.4%)	
Partial hepatectomy	5904 (79.2%)	5521 (79.2%)	383 (79.6%)	
Approach				0.16
Open	6935 (93.1%)	6495 (93.2%)	440 (91.5%)	
MIS	517 (6.9%)	476 (6.8%)	41 (8.5%)	

AA, African American; *IQR*, interquartile range; *MIS*, minimally invasive surgery

Table 2 Perioperative and postoperative outcomes of patients who underwent a hepatectomy stratified by presence of cirrhosis

Complication	Total $N = 7452$	No cirrhosis $N = 6971$	Cirrhosis $N = 481$	p
Outcomes at index visit				
Any complication	1671 (22.4%)	1555 (22.3%)	116 (24.1%)	0.36
Complications				
Pulmonary failure	591 (7.9%)	544 (7.8%)	47 (9.8%)	0.14
Pneumonia	119 (1.6%)	110 (1.6%)	9 (1.9%)	0.57
Myocardial infarction	88 (1.2%)	85 (1.2%)	3 (0.6%)	0.38
DVT/PE	233 (3.1%)	225 (3.2%)	8 (1.7%)	0.06
Acute renal failure	899 (12.1%)	833 (11.9%)	66 (13.7%)	0.25
Hemorrhage	107 (1.4%)	102 (1.5%)	5 (1.0%)	0.56
Surgical site infection	525 (7.0%)	496 (7.1%)	29 (6.0%)	0.41
GI hemorrhage	22 (0.3%)	22 (0.3%)	0 (0.0%)	0.40
Index LOS (median, IQR)	6 (4, 9)	6 (4, 9)	6 (4, 8)	< 0.001
Discharge destination				0.25
Home	4217 (56.6%)	3938 (56.5%)	279 (58.0%)	
SNF	855 (11.5%)	804 (11.5%)	51 (10.6%)	
Home healthcare	1744 (23.4%)	1648 (23.6%)	96 (20.0%)	
Other	636 (8.5%)	581 (8.3%)	55 (11.4%)	
30-day outcomes				
Complications				
Pulmonary failure	101 (1.4%)	91 (1.3%)	10 (2.1%)	0.15
Pneumonia	42 (0.6%)	39 (0.6%)	3 (0.6%)	0.75
Myocardial infarction	25 (0.3%)	23 (0.3%)	2 (0.4%)	0.67
DVT/PE	78 (1.0%)	72 (1.0%)	6 (1.2%)	0.64
Acute renal failure	178 (2.4%)	158 (2.3%)	20 (4.2%)	0.013
Hemorrhage	41 (0.6%)	37 (0.5%)	4 (0.8%)	0.34
Surgical site infection	409 (5.5%)	379 (4.54%)	30 (6.2%)	0.47
GI hemorrhage	23 (0.3%)	22 (0.3%)	1 (0.2%)	1.00
Readmission	1173 (15.7%)	1090 (15.6%)	83 (17.3%)	0.35
Mortality	381 (5.1%)	351 (5.0%)	30 (6.2%)	0.25
90-day outcomes				
Complications				
Pulmonary failure	165 (2.2%)	152 (2.2%)	13 (2.7%)	0.42
Pneumonia	80 (1.1%)	74 (1.1%)	6 (1.2%)	0.65
Myocardial infarction	28 (0.4%)	27 (0.4%)	1 (0.2%)	0.74
DVT/PE	121 (1.6%)	113 (1.6%)	8 (1.7%)	0.85
Acute renal failure	294 (3.9%)	269 (3.9%)	25 (5.2%)	0.15
Hemorrhage	65 (0.9%)	59 (0.8%)	6 (1.2%)	0.31
Surgical site infection	518 (7.0%)	476 (6.8%)	42 (8.7%)	0.11
GI hemorrhage	39 (0.5%)	36 (0.5%)	3 (0.6%)	0.74
Readmission	1867 (25.1%)	1744 (25.0%)	123 (25.6%)	0.79
Mortality	643 (8.6%)	593 (8.5%)	50 (10.4%)	0.15

DVT/PE, deep vein thrombosis/pulmonary embolism; *GI*, gastrointestinal; *LOS*, length-of-stay; *SNF*, skilled nursing facility

discharge destination (e.g., home vs non-home) was similar irrespective of the presence or absence of cirrhosis ($p = 0.25$) with more than one-third of patients ($N = 2599$, 34.9%) requiring discharge to SNF or home with home healthcare following hepatectomy.

Effect of MIS on Perioperative Outcomes

On bivariate analysis, MIS hepatectomy was associated with reduced incidence of prolonged LOS compared with open hepatectomy (OR 0.75, 95% CI 0.59–0.95) (Table 3).

Table 3 Bivariate odds ratio of postoperative outcomes relative to MIS vs open

Outcome	OR	95% CI
Any complication at index visit	0.84	0.67–1.05
LOS ≥ 10 days	0.75	0.59–0.95
Readmission 30 days	0.95	0.73–1.22
Readmission 90 days	1.07	0.87–1.32
Mortality 30 days	0.86	0.53–1.32
Mortality 90 days	0.83	0.57–1.17

LOS, length-of-stay

After stratifying by the presence or absence of cirrhosis, MIS hepatectomy was associated with reduced odds of extended LOS (cirrhosis, OR 0.33, 95% CI 0.06–1.03 vs non-cirrhosis, OR 0.79, 95% CI 0.62–0.99) (Fig. 1). In contrast, MIS hepatectomy was not associated with a reduced incidence of complications, 30- and 90-day readmission, or 30- and-90-day mortality (all $p > 0.05$).

Discussion

Over the past 30 years, the incidence of liver cirrhosis has increased steadily in the USA. Interestingly, cirrhosis-related mortality has decreased by 22% over the same period.[29] Of note, the proportion of elderly patients with cirrhosis undergoing hepatic resection for both benign and malignant diseases is expected to increase.[30] Owing to improvements in surgical techniques and perioperative care, liver resection, in the form of partial hepatectomy or hemi-hepatectomy, is now associated with acceptable outcomes in patients with and without cirrhosis.[5,11,12] Although the impact of cirrhosis on outcomes has been previously reported, there is a paucity of data regarding the influence of cirrhosis on outcomes among elderly patients who underwent hepatectomy. The current study noted that approximately 1 in 4 elderly patients who underwent a hepatectomy suffered a complication during the index admission irrespective of the presence of cirrhosis (complication rates 24.1% vs 22.3%, $p = 0.36$). Similarly, 30- and 90-day mortality and readmission were also similar among patients with and without cirrhosis (30-day mortality 6.2% vs 5%, $p = 0.25$ and 90-day mortality 10.4% vs 8.5%, $p = 0.15$). Perhaps not surprising, patients who underwent a MIS hepatectomy had decreased odds of experiencing an extended LOS compared with patients who underwent an open hepatectomy irrespective of cirrhosis status.

Hepatectomy in the setting of cirrhosis has increased in number due to acceptable outcomes despite these patients being deemed as being more at high risk.[31] For example, Wu and colleagues reported a significant improvement in early- and long-term results after liver resection among patients with cirrhosis undergoing hepatectomy.[12] Specifically, the authors noted a marked reduction in operative blood loss, need for blood transfusion, and mortality over time.[12] Similarly, in a separate study, Fan et al. examined in-hospital mortality among patients with or without cirrhosis undergoing major hepatectomy for HCC and failed to find a difference between the two groups (13% vs 14%, $p > 0.05$).[5] In the current study, which largely included older Medicare beneficiaries, we similarly noted that the overall incidence of perioperative

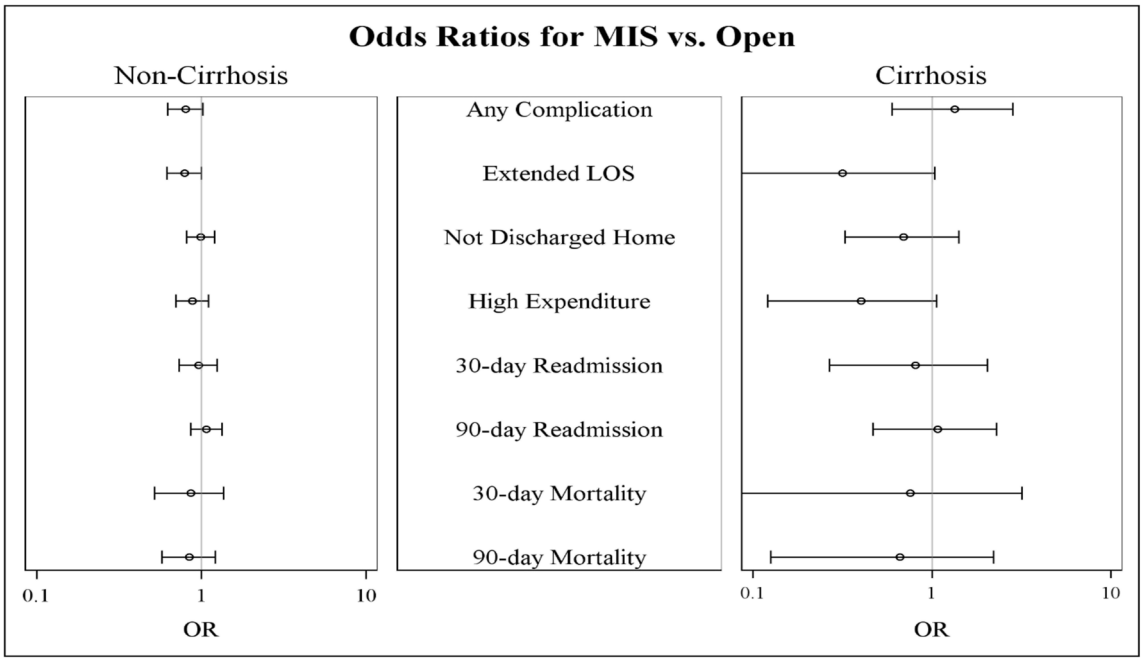

Fig. 1 Forest plot of unadjusted odds ratio of perioperative outcomes after hepatectomy relative to presence of cirrhosis and surgery modality

complications and 30- and 90-day readmission rates were similar among patients regardless of cirrhosis diagnosis.

The safety of hepatic resections in the elderly has been a topic of debate. Elderly patients can exhibit unique age-associated changes in liver function that contribute to reduced hepatic regenerative capacity and decline in liver volume, which may synergistically interact to increase the risk of morbidity following hepatectomy.[32–34] In turn, the risk of hepatectomy among elderly patients with cirrhosis may be particularly risky and associated with increased morbidity. Vitale et al. evaluated perioperative morbidity, mortality, overall survival, and disease-free survival among the elderly versus non-elderly undergoing hepatectomy for intrahepatic cholangiocarcinoma.[35] The authors reported that, while the elderly experienced a higher incidence of complications, long-term outcomes such as disease-free survival and overall survival were comparable with younger patients.[35] Wang et al. argued that elderly people with cirrhosis can derive as much benefit after major hepatectomy for malignant lesions as younger patients.[24] In fact, Wang and colleagues noted similar mortality (1.32% vs 3.57%, $p = 0.63$) and overall complications (47.37% vs 53.57%, $p = 0.42$) among cirrhotic patients undergoing hepatectomy who were < 70 versus ≥ 70 years of age.[24] The current study builds on this previous work and suggested that morbidity following hepatectomy may be acceptable in appropriately chosen patients, as only 1 in 4 elderly patients experienced a complication—which was comparable with the morbidity reported following hepatectomy among younger patients.[36] To this point, Paredes and colleagues have proposed that elderly patients should not be evaluated solely on chronologic age, but rather physiologic age as this latter metric may serve as a better predictor of outcomes.[14] In addition, Menon et al. have noted that clinical factors such as American Society of Anesthesiologist grade 3 may be a better predictor than age alone for overall survival.[13]

Several studies have investigated the impact of MIS on the postoperative outcomes of cirrhotic patients undergoing hepatectomy. These reports have suggested that laparoscopic hepatectomy was superior to open approach in terms of complication rates, blood loss, need for transfusion, and LOS.[8,19,20,23,37–40] Of note, a recent meta-analysis that incorporated data from 9527 laparoscopic liver resections demonstrated that laparoscopy was associated with fewer complications, blood loss, transfusions, and shorter LOS.[22] In addition, MIS has been reported to reduce rates of pulmonary complications and LOS in elderly patients undergoing hepatectomy.[9,41] For example, Nomi et al. noted that elderly patients undergoing laparoscopic major hepatectomy for colorectal liver metastases had comparable postoperative mortality, complications, and major complications versus younger patients.[42] Nevertheless, no previous study had examined the impact of MIS on perioperative outcomes among elderly cirrhotic patients. The current study was important because we specifically investigated elderly patients undergoing MIS. Of interest, elderly patients with and without cirrhosis who had an MIS approach were less likely to experience an extended LOS (non-cirrhotics: OR 0.75, 95% CI 0.59–0.95; cirrhotics: OR 0.33, 95% CI 0.06–1.03); however, there was no difference in complications and 30- and 90-day readmission or mortality among elderly patients who underwent MIS or open surgery.

The current study had several limitations that should be considered when interpreting the results. Although the SAFs provided a large national dataset on claims for Medicare beneficiaries, the data did not reflect all clinical and socioeconomic variables that may have influenced postoperative outcomes such as extent of coagulopathy and liver function. In particular, clinical variables associated with degree of liver cirrhosis were not available. To minimize possible differences due to underlying baseline characteristics, the Charlson comorbidity index score was determined for each patient and controlled for in the multivariable analyses. Complication codes that had a high sensitivity and specificity for identifying postoperative complications among surgical patients were alThe presence of cirrhosis so used. Despite this, similar to other administrative database analyses, there may have been variations in coding that influenced the results.

In conclusion, the presence of cirrhosis did not generally impact outcomes in elderly patients undergoing hepatectomy for benign and malignant diseases. MIS hepatectomy in the elderly Medicare beneficiary population reduced LOS among patients without cirrhosis, yet was not associated with differences in serious morbidity or 30- and 90-day mortality. These findings strongly suggest that cirrhosis should not serve as an absolute contraindication to hepatic resection in elderly patients.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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References

1. Ali N, O'Rourke C, El-Hayek K, Chalikonda S, Jeyarajah DR, Walsh RM. Estimating the need for hepato-pancreatico-biliary surgeons in the USA. HPB : the official journal of the International Hepato Pancreato Biliary Association. 2015;17(4):352–6. doi: https://doi.org/10.1111/hpb.12370.
2. Setiawan VW, Stram DO, Porcel J, Lu SC, Le Marchand L, Noureddin M. Prevalence of chronic liver disease and cirrhosis by underlying cause in understudied ethnic groups: The multiethnic cohort. Hepatology. 2016;64(6):1969–77. doi:https://doi.org/10.1002/hep.28677.
3. Zerillo J, Agarwal P, Poeran J, Zubizarreta N, Poultsides G, Schwartz M et al. Perioperative Management in Hepatic Resections: Comparative Effectiveness of Neuraxial Anesthesia

and Disparity of Care Patterns. Anesthesia and analgesia. 2018;127(4):855–63. doi:https://doi.org/10.1213/ane.0000000000003579.
4. Bell BP, Manos MM, Zaman A, Terrault N, Thomas A, Navarro VJ et al. The epidemiology of newly diagnosed chronic liver disease in gastroenterology practices in the United States: results from population-based surveillance. The American journal of gastroenterology. 2008;103(11):2727–36; quiz 37. doi:https://doi.org/10.1111/j.1572-0241.2008.02071.x.
5. Fan ST, Lai EC, Lo CM, Ng IO, Wong J. Hospital mortality of major hepatectomy for hepatocellular carcinoma associated with cirrhosis. Archives of surgery (Chicago, Ill : 1960). 1995;130(2):198–203.
6. Gozzetti G, Mazziotti A, Cavallari A, Bellusci R, Bolondi L, Grigioni W et al. Clinical experience with hepatic resections for hepatocellular carcinoma in patients with cirrhosis. Surgery, gynecology & obstetrics. 1988;166(6):503–10.
7. Nagasue N, Kohno H, Chang YC, Taniura H, Yamanoi A, Uchida M et al. Liver resection for hepatocellular carcinoma. Results of 229 consecutive patients during 11 years. Annals of surgery. 1993;217(4):375–84.
8. Xu HW, Liu F, Li HY, Wei YG, Li B. Outcomes following laparoscopic versus open major hepatectomy for hepatocellular carcinoma in patients with cirrhosis: a propensity score-matched analysis. Surgical endoscopy. 2018;32(2):712–9. doi:https://doi.org/10.1007/s00464-017-5727-2.
9. Cauchy F, Fuks D, Nomi T, Dokmak S, Scatton O, Schwarz L et al. Benefits of Laparoscopy in Elderly Patients Requiring Major Liver Resection. Journal of the American College of Surgeons. 2016;222(2):174–84.e10. doi:https://doi.org/10.1016/j.jamcollsurg.2015.11.006.
10. Schmucker DL. Age-related changes in liver structure and function: Implications for disease ? Exp Gerontol. 2005;40(8-9):650-9. doi:https://doi.org/10.1016/j.exger.2005.06.009.
11. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK et al. Extended hepatic resection for hepatocellular carcinoma in patients with cirrhosis: is it justified? Annals of surgery. 2002;236(5):602-11. doi:https://doi.org/10.1097/01.sla.0000033038.38956.5e.
12. Wu CC, Cheng SB, Ho WM, Chen JT, Liu TJ, P'Eng F K. Liver resection for hepatocellular carcinoma in patients with cirrhosis. The British journal of surgery. 2005;92(3):348–55. doi:https://doi.org/10.1002/bjs.4838.
13. Menon KV, Al-Mukhtar A, Aldouri A, Prasad RK, Lodge PA, Toogood GJ. Outcomes after major hepatectomy in elderly patients. Journal of the American College of Surgeons. 2006;203(5):677–83. doi:https://doi.org/10.1016/j.jamcollsurg.2006.07.025.
14. Paredes AZ, Beal EW, Bagante F, Dillhoff ME, Cloyd JM, Pawlik TM. Patterns of readmission among the elderly after hepatopancreatobiliary surgery. American journal of surgery. 2018. doi:https://doi.org/10.1016/j.amjsurg.2018.09.011.
15. Gani F, Cerullo M, Amini N, Buettner S, Margonis GA, Sasaki K et al. Frailty as a Risk Predictor of Morbidity and Mortality Following Liver Surgery. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2017;21(5):822–30. doi:https://doi.org/10.1007/s11605-017-3373-6.
16. Li J, Shen Y, Tan L, Feng M, Wang H, Xi Y et al. Is minimally invasive esophagectomy beneficial to elderly patients with esophageal cancer? Surgical endoscopy. 2015;29(4):925–30. doi:https://doi.org/10.1007/s00464-014-3753-x.
17. Fan CJ, Chien HL, Weiss MJ, He J, Wolfgang CL, Cameron JL et al. Minimally invasive versus open surgery in the Medicare population: a comparison of post-operative and economic outcomes. Surgical endoscopy. 2018;32(9):3874–80. doi:https://doi.org/10.1007/s00464-018-6126-z.
18. Clark JR, Wills VL, Hunt DR. Cirrhosis and laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech. 2001;11(3):165–9.
19. Yoon YI, Kim KH, Kang SH, Kim WJ, Shin MH, Lee SK et al. Pure Laparoscopic Versus Open Right Hepatectomy for Hepatocellular Carcinoma in Patients With Cirrhosis: A Propensity Score Matched Analysis. Annals of surgery. 2017;265(5):856–63. doi:https://doi.org/10.1097/sla.0000000000002072.
20. Chen J, Bai T, Zhang Y, Xie ZB, Wang XB, Wu FX et al. The safety and efficacy of laparoscopic and open hepatectomy in hepatocellular carcinoma patients with liver cirrhosis: a systematic review. International journal of clinical and experimental medicine. 2015;8(11):20679–89.
21. Tsilimigras DI, Moris D, Vagios S, Merath K, Pawlik TM. Safety and oncologic outcomes of robotic liver resections: A systematic review. J Surg Oncol. 2018;117(7):1517–30. doi:https://doi.org/10.1002/jso.25018.
22. Ciria R, Cherqui D, Geller DA, Briceno J, Wakabayashi G. Comparative Short-term Benefits of Laparoscopic Liver Resection: 9000 Cases and Climbing. Annals of surgery. 2016;263(4):761–77. doi:https://doi.org/10.1097/sla.0000000000001413.
23. Cheung TT, Dai WC, Tsang SH, Chan AC, Chok KS, Chan SC et al. Pure Laparoscopic Hepatectomy Versus Open Hepatectomy for Hepatocellular Carcinoma in 110 Patients With Liver Cirrhosis: A Propensity Analysis at a Single Center. Annals of surgery. 2016;264(4):612–20. doi:https://doi.org/10.1097/sla.0000000000001848.
24. Wang WL, Zhu Y, Cheng JW, Li MX, Xia JM, Hao J et al. Major hepatectomy is safe for hepatocellular carcinoma in elderly patients with cirrhosis. European journal of gastroenterology & hepatology. 2014;26(4):444–51. doi:https://doi.org/10.1097/meg.0000000000000046.
25. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Medical care. 2005;43(11):1130–9.
26. Iezzoni LI, Daley J, Heeren T, Foley SM, Fisher ES, Duncan C et al. Identifying complications of care using administrative data. Medical care. 1994;32(7):700–15.
27. Osborne NH, Nicholas LH, Ryan AM, Thumma JR, Dimick JB. Association of hospital participation in a quality reporting program with surgical outcomes and expenditures for Medicare beneficiaries. Jama. 2015;313(5):496–504. doi:https://doi.org/10.1001/jama.2015.25.
28. Iezzoni LI, Daley J, Heeren T, Foley SM, Hughes JS, Fisher ES et al. Using administrative data to screen hospitals for high complication rates. Inquiry : a journal of medical care organization, provision and financing. 1994;31(1):40–55.
29. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med. 2014;12:145. doi:https://doi.org/10.1186/s12916-014-0145-y.
30. Petrowsky H, Clavien PA. Should we deny surgery for malignant hepato-pancreatico-biliary tumors to elderly patients? World journal of surgery. 2005;29(9):1093–100. doi:https://doi.org/10.1007/s00268-005-1130-6.
31. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK et al. 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. Annals of surgery. 2004;240(4):698–708; discussion -10.
32. Müller-Höcker J, Aust D, Rohrbach H, Napiwotzky J, Reith A, Link TA et al. Defects of the respiratory chain in the normal human liver and in cirrhosis during aging. Hepatology. 1997;26(3):709–19. doi:https://doi.org/10.1002/hep.510260324.
33. Brouwer A, Barelds RJ, Knook DL. Age-related changes in the endocytic capacity of rat liver Kupffer and endothelial cells. Hepatology. 1985;5(3):362–6.

34. Sastre J, Pallardó FV, Plá R, Pellín A, Juan G, O'Connor JE et al. Aging of the liver: age-associated mitochondrial damage in intact hepatocytes. Hepatology. 1996;24(5):1199–205. doi:https://doi.org/10.1002/hep.510240536.
35. Vitale A, Spolverato G, Bagante F, Gani F, Popescu I, Marques HP et al. A multi-institutional analysis of elderly patients undergoing a liver resection for intrahepatic cholangiocarcinoma. J Surg Oncol. 2016;113(4):420–6. doi:https://doi.org/10.1002/jso.24148.
36. Zhang X-F, Bagante F, Chakedis J, Moris D, Beal EW, Weiss M et al. Perioperative and Long-Term Outcome for Intrahepatic Cholangiocarcinoma: Impact of Major Versus Minor Hepatectomy. Journal of Gastrointestinal Surgery. 2017;21(11):1841–50. doi:https://doi.org/10.1007/s11605-017-3499-6.
37. Cheung TT, Poon RT, Yuen WK, Chok KS, Jenkins CR, Chan SC et al. Long-term survival analysis of pure laparoscopic versus open hepatectomy for hepatocellular carcinoma in patients with cirrhosis: a single-center experience. Annals of surgery. 2013;257(3):506-11. doi:https://doi.org/10.1097/SLA.0b013e31827b947a.
38. Belli G, Fantini C, D'Agostino A, Cioffi L, Langella S, Russolillo N et al. Laparoscopic versus open liver resection for hepatocellular carcinoma in patients with histologically proven cirrhosis: short- and middle-term results. Surgical endoscopy. 2007;21(11):2004–11. doi:https://doi.org/10.1007/s00464-007-9503-6.
39. Belli G, Limongelli P, Fantini C, D'Agostino A, Cioffi L, Belli A et al. Laparoscopic and open treatment of hepatocellular carcinoma in patients with cirrhosis. The British journal of surgery. 2009;96(9):1041–8. doi:https://doi.org/10.1002/bjs.6680.
40. Kaneko H, Tsuchiya M, Otsuka Y, Yajima S, Minagawa T, Watanabe M et al. Laparoscopic hepatectomy for hepatocellular carcinoma in cirrhotic patients. Journal of hepato-biliary-pancreatic surgery. 2009;16(4):433–8. doi:https://doi.org/10.1007/s00534-009-0123-5.
41. Sucandy I, Cheek S, Tsung A, Marsh JW, Geller DA. Minimally invasive liver resection for primary and metastatic liver tumors: influence of age on perioperative complications and mortality. Surgical endoscopy. 2018;32(4):1885–91. doi:https://doi.org/10.1007/s00464-017-5880-7.
42. Nomi T, Fuks D, Kawaguchi Y, Mal F, Nakajima Y, Gayet B. Laparoscopic major hepatectomy for colorectal liver metastases in elderly patients: a single-center, case-matched study. Surgical endoscopy. 2015;29(6):1368–75. doi:https://doi.org/10.1007/s00464-014-3806-1.