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ABOUT COVER

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WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc*.

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ORIGINAL ARTICLE

Retrospective Study

Impact of body mass index in elderly patients treated with laparoscopic liver resection for hepatocellular carcinoma

Maria Conticchio, Riccardo Inchingolo, Antonella Delvecchio, Francesca Ratti, Maximiliano Gelli, Massimiliano Ferdinando Anelli, Alexis Laurent, Giulio Cesare Vitali, Paolo Magistri, Giacomo Assirati, Emanuele Felli, Taiga Wakabayashi, Patrick Pessaux, Tullio Piardi, Fabrizio di Benedetto, Nicola de'Angelis, Javier Briceño, Antonio Rampoldi, Renè Adam, Daniel Cherqui, Luca Antonio Aldrighetti, Riccardo Memeo

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Abstract

BACKGROUND

The impact of obesity on surgical outcomes in elderly patients candidate for liver surgery is still debated.

AIM

To evaluate the impact of high body mass index (BMI) on perioperative and oncological outcome in elderly patients (> 70 years old) treated with laparoscopic liver resection for hepatocellular carcinoma (HCC).

METHODS

Retrospective multicenter study including 224 elderly patients (> 70 years old) operated by laparoscopy for HCC (196 with a BMI < 30 and 28 with BMI ≥ 30), observed from January 2009 to January 2019.

RESULTS

After propensity score matching, patients in two groups presented comparable results, in terms of operative time (median range: 200 min *vs* 205 min, *P* = 0.7 respectively in non-obese and obese patients), complications rate (22% *vs* 26%, *P* = 1.0), length of hospital stay (median range: 4.5 d *vs* 6.0 d, *P* = 0.1). There are no significant differences in terms of short- and long-term postoperative results.

CONCLUSION

The present study showed that BMI did not impact perioperative and oncologic outcomes in elderly patients treated by laparoscopic resection for HCC.

Key Words: Hepatocellular carcinoma; Body mass index; Laparoscopy; Surgical resection; Elderly patients; Propensity score matching

Core Tip: In order to evaluate the impact of a high body mass index (BMI) in elderly patients who underwent laparoscopic resection for hepatocellular carcinoma (HCC), we compared perioperative data and long-term outcomes from 10 European centers before and after propensity score matching. The present study showed that BMI did not impact perioperative and oncologic outcomes in elderly patients treated by laparoscopic resection for HCC.

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INTRODUCTION

Obesity is a significant contributing factor for the development of liver disease, starting from the stage of non-alcoholic steatohepatitis up to cirrhosis and hepatocellular carcinoma (HCC)[1-4]. Due to the constant increase of population aging, the treatment of HCC in elderly obese patient has become a global clinical issue[5]. Laparoscopic liver resection (LLR) provides the benefits of minimally invasive approach in terms of short-term outcomes[6,7], guaranteeing oncological results comparable to the open surgical approach[8,9]. However, data about the impact of obesity in patients undergoing LLR remain controversial, with some studies reporting higher body mass index (BMI) as a predictor of an adverse postoperative outcome[10] and other studies not reporting an increased risk of postoperative morbidity linked to obesity[11]. The aim of this study was to evaluate the impact of BMI in elderly patients undergoing LLR for HCC, by comparing short- and long-term outcomes.

MATERIALS AND METHODS

This multicenter retrospective study included 224 patients treated between January 2009 and January 2019, at the following centers: Policlinico di Bari, Bari, Italy; Policlinico di Modena, Modena, Italy; Ospedale San Raffaele, Milan, Italy; Grande Ospedale Metropolitano Niguarda, Milan, Italy; Centre hé pato-biliaire Paul Brousse, Villejuif, France; Hôpitaux Universitaires Henri Mondor, Créteil, France; Hospital Universitario Sofía, Córdoba, Spain; Hôpitaux Universitaires de Genève, Geneva, Switzerland; Nouvel Hôpital Civil, Strasbourg, France; Centre Hospitalier Universitaire, Reims, France.

This study investigated patients resected for HCC demonstrating the following inclusion criteria: Child-Pugh class A and B disease; age ≥ 70 years; no evidence of major vessel branch invasion and no distant metastases. Based on the World HealthOrganization (WHO) definition of obesity (BMI > 30 kg/m^2)[12] patients were divided in two groups: BMI < 30 kg/m^2 group and BMI > 30 kg/m^2 group.

The diagnosis of HCC was done, according to the European Association for Study of Liver (EASL) consensus criteria[13], based on non-invasive findings or histopathology. The type of treatment was planned following multidisciplinary tumor board discussions.

LLR procedure

The surgical procedure was planned based on tumor features and liver function. Minor and major liver resections were performed according Brisbane classification[14]. The choice of position and the size of trocars depended by tumor location. Intraoperative ultrasonography represented a standardized initial step of surgical procedure. Liver parenchymal transection was performed with laparoscopic instruments using various energy devices such as the cavitation ultrasonic surgical aspirator ultrasonic, monopolar and bipolar forceps. The extent of resection depended on the size and anatomical location of the tumor and they were defined as "minor" for the resection of two or fewer Couinaud's liver segments, and 'major' for the resection ≥ 3 liver segments. The hepatic hilum was prepared for the Pringle's maneuver. The specimen was placed in an endocatch bag and removed from one of the trocars' incision sites.

Follow-up

Short-term outcomes after liver resection included the evaluation of the parameters in the perioperative period, including intraoperative variables such as operative time, and blood transfusion rate, and postoperative variables as complications rate (based on the Clavien-Dindo classification[15]), and length of hospitalization. Long-term outcomes included oncological results in terms of overall survival and disease-free survival (DFS). Liver blood tests were assessed on first, third and fifth postoperative day. Follow-up was performed once every 3 mo during the first year and every 4 mo thereafter with CT-scan and blood tests (including liver function and oncologic markers). Recurrence after treatment included repeat resection, locoregional treatment, till liver transplantation, or supportive care based on the patient's general status and liver disease according to the EASL-EORTC clinical practice guidelines[13].

Statistical analysis

Statistical analyses were carried out using the IBM SPSS Statistics 20 software. The *t*-test and Mann-Whitney *U* test were used to compare continuous variables. The chi-square test and Kruskal-Wallis test respectively was performed to compare categorical variables. The Kaplan-Meier method was used to assess recurrence-free survival (RFS) and overall survival (OS) curves. The Cox proportional hazard model was performed to analyse independent prognostic factors of longterm survival. A propensity score matching (PSM) analysis was performed to reduce selection bias obtaining two more homogeneous matched groups of patients in the resection and ablation groups. Variables included in our propensity model included age, comorbidities ≥ 2, American Society of Anesthesiologists (ASA) score, Child-Pugh and model for end-stage liver disease (MELD) scores, extent of resection, tumor number and size. A one-to-one PSM was performed with a caliper width of < 0.2 of the pooled standard deviation of estimated propensity scores, applying these variables to a logistic regression model and calculated C-statistics. A total of 27 out of the 196 patients in the BMI < 30 group and a total of 27 out of the 28 patients in the BMI > 30 group were matched for further analyses.

RESULTS

Before PSM

We included 224 patients treated with LLR for an HCC and aged ≥ 70 years. One hundred and ninty-six patients presented a BMI < 30 kg/m^2 and 28 patients presented a BMI > 30 kg/m^2. Demographic data were similar between two groups, except for a higher rate of male in BMI ≥ 30 kg/m^2 group than in BMI < 30 kg/m^2 group (69% *vs* 93%, *P* = 0.001). Associated comorbidities were not increased in obese patients, as ASA and MELD score (Table 1).

Perioperative and postoperative data are described in Table 2. There were no significant differences in surgical time (median range: 200 min *vs* 220 min, *P* = 0.70, in the BMI < 30 and BMI > 30 respectively), rate of blood transfusion (16% *vs* 3%, *P* = 0.09), length of hospitalization (median range: 6.0 d *vs* 5.5 d, *P* = 0.20)

The global rate of postoperative complication was higher in the non-obese group (47% *vs* 25%, *P* = 0.02) compared to the obese group. Only the rate of wound infection was higher in the obese group (11% *vs* 2%, *P* = 0.04).

The 90-d mortality rate didn't present significative difference between the two groups (5% in BMI < 30 group and 0% in BMI > 30 group, *P* = 0.60). The estimated 1- and 3-year OS rates were 100% and 92.3% in BMI > 30 group, and 96% and 91.4% in BMI < 30 group (*P* = 0.004; Figure 1A) respectively. The estimated 1- and 3-year DFS rates were 96% and 67% in BMI > 30 group, and 82% and 36% in BMI < 30 group (*P* = 0.50; Figure 1B) respectively.

After PSM

After matching, we obtained a more homogeneous population for both groups (Table 1). The variables included in the PSM were age, comorbidities, ASA and MELD score, Child Pugh score, tumor size, tumor number and extent of resection. Peri-operative and post-operative results are analytically described in Table 2. The post-operative follow up didn't reveal any difference in the complication's rate between BMI > 30 and BMI < 30 group (26% *vs* 22%, *P* = 1.0), nor in grade of severity (Clavien-Dindo grades III-IV) (4% *vs* 7% *P* = 0.6). Moreover, operative time (median range: 205 min *vs* 200 min, *P* = 0.7) and rate of blood transfusion (3% *vs* 18%, *P* = 0.2) were similar. The estimated 1- and 3-year overall survival rates were 100% and 92.3% in the BMI > 30 group, and 88.4% and 83.5% in the BMI < 30 group (*P* = 0.2; Figure 1C).

The estimated 1- and 3-year DFS rates were 96.2% and 65.8% in the BMI > 30 group, and 87.5% and 86.2% in the BMI < 30 group (*P* = 0.5; Figure 1D) respectively.

DISCUSSION

The impact of obesity on surgical results in elderly patients who underwent liver resections remains a subject of vivid debate. An increased surgical risk has been expected because of comorbidities, associated to obesity and old age, underlying liver disease and technical difficulties[16-20]. Our multicenter study did not confirm this hypothesis and showed that LLR can be safely performed in treatment of HCC also in elderly patients with a BMI ≥ 30 kg/m^2. The evaluation of the influence of BMI in elderly population is important because of the increasing prevalence of this condition associated to an higher average life expectancy[21,22].

The increasing BMI has been reported as a predisposition to develop various diseases, including diabetes mellitus, hypertension, respiratory disease and certain type of cancers[23-25]. Our data did not show differences in term of rate of comorbidities or tumor characteristics, even after PMS analysis, according to various preoperative parameters (age, comorbidities, ASA and MELD score, Child Pugh score, tumor size, and tumor number and extent of resection), which resulted in a more homogeneous and therefore comparable population.

Even though the initial hypothesis that obesity negatively affected the outcomes of minimally invasive approach was not verified[26], data regarding LLR in obese patients were controversial. After the evaluation of surgical procedures ended with Second International Consensus Conference on LLR [27], a scoring system was built to stratify LLR into groups with increasing degree of difficulty[28]. This IWATE score aimed to preoperatively predict, the technical difficulty of various LLR, but without including body habitus. So, the question whether anthropometric variables really have an impact on perioperative outcomes, remains.

Using operative time, rate of blood transfusion and rate of conversion as surrogates of surgical difficulty, Ome *et al*[29] reported significantly longer median operation time in obese compared to non-obese patients, while for Uchida *et al*[30] BMI was an independent predictor of longer operative time > 200 min. Lee *et al*[31] reported a significant difference in operative time and incidence of blood transfusion in overweight compared to normal weight patients, but no difference for obese patients. In accordance to the abovementioned data, the results of this study also suggest similar rate of blood transfusion and operative time in patients with BMI < 30 kg/m^2 and those with BMI ≥ 30 kg/m^2.

The advantages of a minimally invasive approach in liver surgery, including lower abdominal wall morbidity and early postoperative rehabilitation[32,33], may be more beneficial for the subgroup of obese patients. A recent systematic review[34] reported similar rates of postoperative complications between obese and non-obese patients, although several issues including discrepancy in the obesity definition, limit the validity of these results. Nomi *et al*[35] reported that the postoperative course of obese patients was not negatively affected by a higher incidence of infectious complications nor liver

Table 1 Preoperative and clinical characteristics of elderly patients with hepatocellular carcinoma with a body mass index < 30 or ≥ 30 who underwent laparoscopic liver resection

	LLR before PSM (224)			After PSM (54)		
	BMI < 30 (196)	BMI ≥ 30 (28)	*P*	BMI < 30 (27)	BMI ≥ 30 (27)	*P*
MALE	135 (69)	26 (93)	0.00	17	25	0.02
Age (yr), median (range)	75.2 (69.5-90.0)	75.3 (69.7-86.6)	0.70	76.3 (70.6-81.2)	73.1 (70-82.3)	0.70
BMI (kg/cm²), median (range)	26.7 (19.0-29.0)	32.5 (30.0-52.0)	0.00	26.7 (25.0-267.0)	33 (30-37)	
Co-morbidities > 2, *n* (%)	77 (80)	9 (32)	0.50	14	9	0.27
Cause of Cirrhosis, *n* (%)						
Hepatitis C virus	102 (52)	12 (43)	0.40	16	11	0.27
Hepatitis B virus	39 (20)	4 (14)	0.60	7	4	0.50
Alcohol	23 (12)	7 (25)	0.07	1	7	0.05
Others	32 (16)	5 (18)	0.80	3	5	0.70
ASA score, *n* (%)			0.80			1.00
I-II	84 (43)	11 (39)		10	10	
III-IV	112 (57)	17 (61)		17	17	
Blood tests median (range)						
Bilirubin (mg/dL)	0.9 (0.2-4.2)	0.9 (0.2-2.1)	0.8	0.9 (0.3-1.1)	0.5 (0.2-1.1)	0.70
Creatinine (mg/dL)	0.9 (0.2-2.5)	0.9 (0.4-1.9)	1.00	0.9 (0.8-1.5)	0.9 (0.7-2)	0.80
Platelet count, × 10^9/L	176 (45-421)	187 (72-468)	0.3	144 (47-337)	168 (117-396)	0.80
INR	1.1 (0.6-2.0)	1.08 (0.7-1.67)	0.3	1.1 (1-1.5)	1 (1-1.3)	0.50
CHILD-PUGH, *n* (%)			0.2			1.00
A	177 (90)	23 (82)		23	22	
B	19 (68)	5 (18)		4	5	
MELD median (range)	6 (6-16)	6 (6-13)	0.6	8 (6-12.5)	8 (6-13)	0.40
Tumors number *n* (%)			0.06			1.00
Single nodule	191 (97)	25 (89)		24	24	
Multi nodules	5 (3)	3 (11)		3	3	
Tumors size (mm), median (range)	30 (9-50)	30 (18-50)	0.6	30 (9-50)	27 (24-35)	0.30
Bilobar tumor, *n* (%)	1 (0.5)	1 (3)	0.2	1	1	1.00
Tumor in PS segment, *n* (%)	41 (21)	6 (21)	1.00	5	5	1.00
Histologically proven *n* (%)	31 (16)	8 (29)	0.11			
Previous treatment, *n* (%)	12 (6)	3 (10)	0.4			
Major hepatectomy, *n* (%)	22 (11)	2 (7)	0.7	1	2	1.00
Operative time > 240 min	73 (37)	12 (43)	0.7	150 (80-210)	150 (65-155)	0.70

Continuous variables were compared using an independent sample *t*-test and Mann-Whitney *U* test. Categorical variables were compared using the chi-square test and Kruskal-Wallis test respectively. LLR: Laparoscopic liver resection; PSM: Propensity score matching; HCC: Hepatocellular carcinoma; BMI: Body mass index; ASA: American Society of Anesthesiologists; MELD: Model for End Stage Liver Disease.

specific complications. Yu *et al*[36] reported a higher rate of bile leak in obese compared to non-obese patients. The herein presented data demonstrate a similar postoperative outcome, with no significant differences in major complications (Clavien Dindo III-IV) nor liver related complications in obese compared to non-obese patients.

View magnification of, optimal exposure with liver mobilization and the increase of dedicated tools allow a clearer visualization of deep structures, small vessels and biliary ducts[7,36,37]. The authors speculate this "power" of laparoscopy can justify a lower rate of postoperative complications not only in

Table 2 Preoperative and clinical characteristics of elderly patients with hepatocellular carcinoma with a 30 > body mass index ≥ 30 who underwent laparoscopic liver resection

	LLR before PSM (224)			After PSM (54)		
	BMI < 30 (196)	BMI ≥ 30 (28)	*P*	BMI < 30 (27)	BMI ≥ 30 (27)	*P*
Operative time (min), median (range)	200 (70-600)	220 (65-337)	0.70	200 (80-320)	205 (65-337)	0.7
Blood transfusion, *n* (%)	32 (16)	1 (3)	0.09	5 (18)	1 (3)	0.2
Dindo-Clavien classification, *n* (%)			0.23			0.6
I-II	18 (92)	27 (97)		23 (93)	26 (96)	
III-IV	16 (8)	1 (3)		2 (7)	1 (4)	
Postoperative complications, *n* (%)			0.02			1.0
Yes	93 (47)	7 (25)		6 (22)	7 (26)	
No	103 (53)	21 (75)		21 (78)	20 (74)	
Type of complication, *n* (%)						
Liver failure	15 (8)	1 (3)	0.70	2 (7)	1 (4)	1.0
Ascites	24 (12)	2 (7)	0.70	3 (11)	2 (7)	1.0
Biliary leakage	2 (1)	1 (3)	0.30	0	1 (4)	1.0
Hemorrhage	8 (4)	0	0.60	2 (7)	0	0.5
Systemic infection	14 (7)	1 (3)	0.70	2 (7)	1 (4)	1.0
Intra-abdominal abscess	7 (3)	0	0.60	2 (7)	1 (4)	1.0
Wound infection	4 (2)	3 (11)	0.04	0	3 (11)	0.2
Portal thrombosis	2 (1)	0	1.00	1 (4)	0	1.0
Pulmonary	15 (7)	0	0.20	2 (7)	0	0.5
Cardiac	11 (5)	1 (3)	1.00	2 (7)	1 (4)	1.0
Renal	8 (4)	0	0.60	2 (7)	0	0.5
Reoperation, *n* (%)	6 (6)	1 (3)	1.00	0	1 (4)	1.0
Postoperative death, *n* (%)	7 (3)	0	0.60	2 (7)	0	0.5
Postoperative treatment, *n* (%)	6 (3)	1 (3)	1.00	0	1 (4)	1.0
Length of hospital stay, median (range)	6 (2-40)	5.5 (3-21)	0.20	4.5 (2-40)	6 (3-21)	0.1
Mortality at 90 d, *n* (%)	9 (5)	0	0.60	2 (7)	0	0.5

Continuous variables were compared using an independent sample *t*-test and Mann-Whitney *U* test. Categorical variables were compared using the chi-square test and Kruskal-Wallis test respectively; LLR: Laparoscopic liver resection; PSM: Propensity score matching; BMI: Body mass index.

terms of preservation of abdominal wall integrity, linked with prevention on respiratory diseases and reduction of postoperative pain, but also with a greater accuracy in resection technique, especially in the hands of experienced surgeons.

Oncological outcomes following PSM were also similar, as no differences were noted in disease-free and overall survival in obese *vs* non-obese patients, undergoing LLR for HCC. This is also in accordance with in the majority of published data[34]. These results suggest that also elderly obese patients can benefit from surgical treatment in terms of long-term outcomes, mainly driven by the excellent short-term outcome of laparoscopy.

CONCLUSION

In conclusion, according to the present study, BMI does not impact surgical outcomes of LLR in elderly patients treated for HCC. Thorough patient selection, based on liver volume and function evaluation, as well as patient habitus and comorbidities, could result in safe and feasible LLR in elderly obese patients.

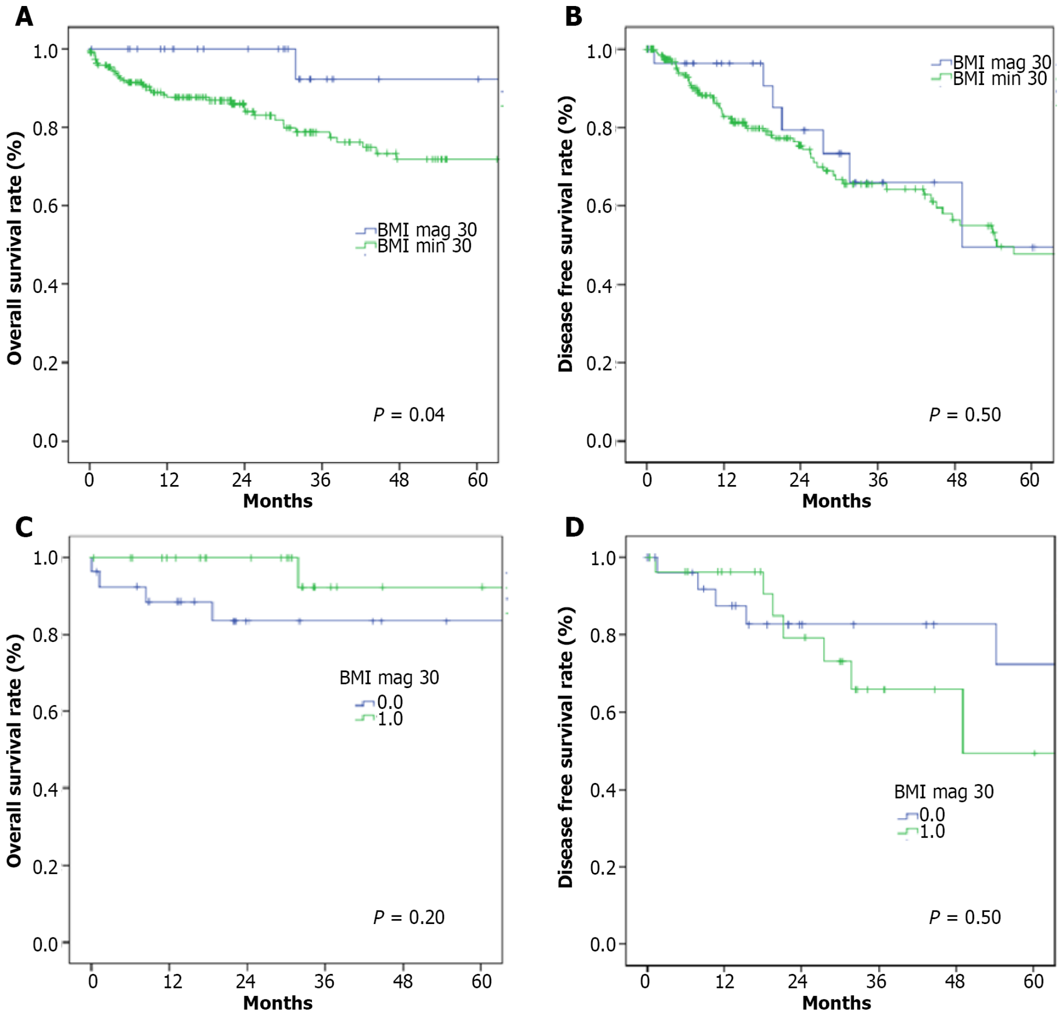

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Figure 1 Survival curves and Tumor recurrence curves (Kaplan-Meier method) of elderly patients with hepatocellular carcinoma with a 30 > body mass index ≥ 30 who underwent laparoscopic liver resection before propensity score matching. A: Overall survival (OS) curves were constructed using the Kaplan-Meier method and compared using the log-rank test, OS significantly did not differ between the two groups; B: Recurrence-free survival (RFS) curves were constructed using the Kaplan-Meier method and compared using the log-rank test, hepatocellular carcinoma recurrence significantly differs between the two groups; C: OS curves were constructed using the Kaplan-Meier method and compared using the log-rank test; after propensity score matching, survival remained significantly different; D: RFS curves were constructed using the Kaplan-Meier method and compared using the log-rank test; after propensity score matching, recurrence remained significantly different. BMI: Body mass index.

ARTICLE HIGHLIGHTS

Research background

A high body mass index (BMI) could represent a factor which impacts perioperative outcomes in elderly patients who underwent laparoscopic liver resection (LLR).

Research motivation

To evaluate of postoperative outcomes between elderly (age > 70 years) patients with a BMI ≥ 30 and BMI < 30 who underwent a LLR for hepatocellular carcinoma (HCC).

Research objectives

The analysis of short (perioperative) and long-term (oncological results) outcomes.

Research methods

The analysis of data was performed before and after propensity score matching.

Research results

After propensity score matching, patients in two groups presented comparable results, in terms of operative time complications rate length of hospital stay. There are no significant differences in terms of short- and long-term postoperative results.

Research conclusions

The present study showed that BMI did not impact perioperative and oncologic outcomes in elderly patients treated by laparoscopic resection for HCC.

Research perspectives

Randomized controlled studies are needed to better explore these results.

FOOTNOTES

Author contributions: Conticchio M, Inchingolo R, Delvecchio A, Ratti F, Gelli M, Anelli MF, Laurent A, Vitali GC, Magistri P, Assirati G, Felli E, Wakabayashi T, Pessaux P, Piardi T, di Benedetto F, de'Angelis N, Briceño J, Rampoldi A, Adam R, Cherqui D, Aldrighetti LA, and Memeo R equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

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