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Body Mass Index and Waistline are Predictors of Survival for Hepatocellular Carcinoma After Hepatectomy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide especially in China. This article aimed to evaluate the influence of body mass index (BMI) and waistline on complications, postoperative death, and long-term survival in patients undergoing surgery for HCC.

Material/Methods: 136 patients were enrolled and divided into 4 groups: group A, BMI <25; group B, BMI ≥25; group C, waistline <90 cm in males or waistline <80 cm in females; group D, waistline ≥90 cm in males or waistline ≥80 cm in females. Clinical pathological features and surgical outcomes of these patients were analyzed retrospectively.

Results: There were no significant differences in postoperative complication rate and postoperative death between group A and group B, although pulmonary infection showed a significant difference between 2 groups ($P=0.017$). Vascular invasion, waistline, and BMI are the independent prognostic factors for long-term survival. The disease-free survival curves after hepatectomy showed no statistically significant difference between group A and group B. Group C had the better overall survival than group D, and group A had the better overall survival than group B.

Conclusions: BMI and waistline are both independent prognostic factors for long-term survival of HCC after hepatectomy. Waistline is more important than BMI in predicting the disease-free survival of HCC after hepatectomy.

MeSH Keywords: **Body Mass Index • Carcinoma, Hepatocellular • Patient Outcome Assessment**

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Background

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide especially in China [1–3]. The high HCC rates in China largely reflect the elevated prevalence of chronic hepatitis B virus (HBV) infection. In developed countries such as United States, nonalcoholic fatty liver disease (NAFLD), associated with obesity, are thought to account for the majority of HCC [4–6]. However, nowadays, obesity is becoming a serious problem in China. Less study focused on the effect of obesity on HCC especially in the relationship between BMI and HCC. No study has focused on the effect of waistline on the surgical outcome of HCC patients. So, this study is about the influence of body mass index (BMI) and waistline on complications, postoperative death and long-time survival in patients undergoing surgery for HCC.

Material and Methods

Between January 2007 and December 2012, we retrospectively reviewed the database of 136 patients underwent hepatic resection for HCC at the Department of Surgery of the Fourth Affiliated Hospital of Zhejiang University School of Medicine. This retrospective study had been performed with the approval of the ethics committee of the Fourth Affiliated Hospital of Zhejiang University School of Medicine and was in compliance with the Helsinki Declaration. Written informed consent was given by participants for their clinical records to be used in this study. Patient records/information was anonymized and de-identified prior to analysis. BMI and waistline measurement was carried out on the day of admission. We enrolled 136 patients and divided them into 4 groups: group A, BMI <25; group B, BMI ≥25; group C, waistline <90 cm in males or waistline <80 cm in females; group D, waistline ≥90 cm in males or waistline ≥80 cm in females. There were 61 patients (44.9%) in group A, 75 patients (55.1%) in group B, 58 patients (42.6%) in group C, and 78 patients (57.4%) in group D.

All patients followed the same preoperative evaluation protocol, including blood biochemistry, ultrasonography, and computed tomography of the liver. The criteria for resection included good general condition, absence of essential organ dysfunction and distant metastasis, and liver function (Child A or B, ICG R15 <15%). All intraoperative and postoperative complications were recorded retrospectively. Follow-up data were obtained by direct communication with patients after they underwent hepatic resection.

Linear data are expressed as mean ±SD. Linear data was compared using the independent-samples t test. Survival analysis, including overall survival and disease-free survival, was estimated by the Kaplan-Meier survival method and compared

Table 1. Clinicopathologic features of 136 HCC patients underwent hepatectomy (mean ±SD).

Variables	No. of patients(%)
Gender	
Female	26 (19.1%)
Male	110 (80.9%)
Age (years)	43±9
<60	118 (86.8%)
≥60	18 (13.2%)
BMI	
<25	61 (44.9%)
≥25	75 (55.1%)
Waistline (cm)	
<90 cm in men/ <80 cm in women	58 (42.6%)
≥90 cm in men/ ≥80 cm in women	78 (57.4%)
Hepatitis B status	
Negative	39 (28.7%)
Positive	97 (71.3%)
Capsular formation	
Presence	54 (39.7%)
Absence	82 (60.3%)
Tumor number	
Solitary	51 (37.5%)
Multiple	85 (62.5%)
AFP level	
Negative	48 (35.3%)
Positive	88 (64.7%)
Liver cirrhosis	
Absent	71 (52.2%)
Present	65 (47.8%)
Tumour size (cm)	6.2±3.3
Vascular invasion	
Absent	95 (69.9%)
Present	41 (30.1%)

Table 2. Intraoperative and postoperative data of 136 patients with HCC.

Data	BMI <25 No. of patients (%)	BMI ≥25 No. of Patients (%)	P value
Hospital stay (days)	11 (8–18)	12 (9–21)	0.373
Blood loss (ml)	768±450	798±533	0.335
≥1000	23 (37.7%)	29 (38.7%)	0.909
Hospital mortality	0 (0%)	1 (1.3%)	0.365
Major complications	7 (11.5%)	9 (12%)	0.925
Ascites	2	1	0.375
Wound infection	2	2	0.771
Pulmonary infection	0	5	0.017
Biliary fistula	1	0	0.242
Liver failure	1	1	0.849
Bleeding	1	0	0.242

using the log-rank test. Cox proportional hazard regression analysis was used to identify independent prognostic factors. All statistical analyses were performed using statistical software (SPSS 13.0 for Windows, SPSS, Chicago, IL) at a significant level of $P < 0.05$.

Results

Clinicopathologic features of 136 HCC patients underwent hepatectomy

There were 110 (80.9%) men and 26 (19.1%) women who underwent hepatectomy. The median age was 43 years; 118 (86.8%) patients were ages <60 years and 18 (13.2%) patients were older than 60 years. There were 61 (44.9) patients with normal BMI (<25) and 75 (55.1%) patients were overweight or obese (BMI ≥25). Fifty-eight patients (42.6%) belong to group C and 78 patients (57.4%) belong to group D. Ninety-seven (71.3%) patients had positive hepatitis B and 39 (28.7%) patients without HBV. Eighty-eight (64.7%) patients had positive AFP level. The size of the tumors was 6.2 ± 3.3 cm. Histopathology of the HCC confirmed vascular invasion in 41 patients (30.1%) and liver cirrhosis in 65 (47.8%) patients. Surgical results confirmed capsular formation in 54 (39.7%) patients and 51 (37.5%) patients with solitary HCC (Table 1).

Intraoperative and postoperative data of 136 patients with HCC

The intraoperative and postoperative data including major complications of 136 patients with HCC are shown in Table 2 and

Supplementary Table 1. The median hospital stay was 11 days in group A and 12 days in group B, with no significant difference between the 2 groups ($P=0.373$). Blood loss was unaffected by the BMI ($P=0.335$). In group A, 23 (37.7%) patients had blood loss ≥1000 ml compared to 29 (38.7%) patients in group B. There was no hospital death in group A and 1 (1.3%) hospital death in group B. However, no significant difference was found between the 2 groups. There were no significant differences in overall postoperative complication rate between group A and group B, although pulmonary infection showed a significant difference between these 2 groups ($P=0.017$). Seven (11.5%) patients had complications in group A compared to 9 (12%) patients in group B. The most common complications in group A were ascites and wound infection, while the most common complications in group B were pulmonary infection and wound infection. The only hospital death was attributed to liver failure in a group B patient.

Prognostic factors for HCC after hepatic resection

Variables that might affect overall survival of patients with HCC after hepatic resection were analyzed in this study. On univariate analysis of the prognostic factors, we found that patients with BMI ≥25, waistline ≥90 cm (or ≥80 cm in women) and vascular invasion had poor overall survival than that without these variables ($P=0.032$, $P=0.017$, $P=0.009$). The other variables such as sex, AFP level, and blood loss were not the significant prognostic factors of overall survival. On multivariate analysis, however, only vascular invasion and waistline were significantly associated with overall survival ($P=0.031$, $P=0.039$). The other variables, including BMI, were not independent prognostic factors of overall survival on multivariate analysis (Table 3).

Table 3. The Cox proportional hazard regression analyses for overall survival.

Variables	n*	Univariable analysis		Multivariable analysis	
		HR (95% CI)	P value	HR (95% CI)	P value
Gender					
Female	26	1		1	
Male	110	1.036 (0.608–2.133)	0.370	1.777 (0.390–2.186)	0.457
Age (years)					
<60	118	1		1	
≥60	18	1.008 (0.828–2.317)	0.325	1.133 (0.529–3.906)	0.843
Hepatitis B status					
Positive	97	1		1	
Negative	39	1.541 (0.913–2.600)	0.106	1.199 (0.661–2.176)	0.550
AFP level (ng/mL)					
Negative	48	1		1	
Positive	88	1.003 (0.999–1.006)	0.114	1.213 (0.624–2.537)	0.274
BMI					
<25	61	1		1	
≥25	75	2.285 (1.074–4.863)	0.032	2.410 (0.933–4.316)	0.061
Liver cirrhosis					
Absent	71	1		1	
Present	65	1.260 (0.541–2.933)	0.592	1.536 (0.661–3.367)	0.881
Waistline					
<90 cm in men or <80 cm in women	58	1		1	
≥90 cm in men or ≥80 cm in women	78	2.448 (1.174–5.106)	0.017	2.273 (1.122–6.238)	0.039
Vascular invasion					
Absent	95	1		1	
Present	41	2.639 (1.943–4.045)	0.009	2.015 (1.307–5.678)	0.031
Blood loss (ml)					
<1000	84	1		1	
≥1000	52	1.484 (0.874–2.521)	0.144	1.531 (0.866–3.124)	0.373
Major complications					
Absent	120	1		1	
Present	16	1.142 (0.314–4.156)	0.840	0.615 (0.258–2.467)	0.273

* Number of patients

Long-term survival of HCC patients according to the BMI and waistline

The overall survival curves of HCC patients according to the BMI are shown in Figure 1. The 1-, 3-, and 5-year overall survival rates of group A were 95%, 81%, and 16%, respectively. The 1-, 3-, and 5-year disease-free survival rates of these patients were 78%, 38% and 4%, respectively (Figure 1). Group A

had significantly better overall survival than group B ($P=0.048$). However, there was no significant difference between the 2 groups in disease-free survival ($P=0.235$). The overall and disease-free survival curves of HCC patients affected by waistline were shown in Figure 2. The 1-, 3-, and 5-year overall survival rates of group C were 97%, 88%, respectively, and 15% compared to 96%, 68%, 15%, respectively, in group D. The 1-, 3-, and 5-year disease-free survival rates of group C were 84%, 40% and

Supplementary Table 1. Intraoperative and postoperative data of 136 patients grouped by waistline.

Data	<90 cm in men or <80 cm in women	≥90 cm in men or ≥80 cm in women	P value
Hospital stay (days)	10 (7–20)	13 (10–21)	0.643
Blood loss (ml)	734±523	802±511	0.372
≥1000	22	30	0.283
Hospital mortality	0	1	0.427
Major complications	8	8	0.283
Ascites	2	1	0.109
Wound infection	2	2	0.236
Pulmonary infection	1	4	0.101
Biliary fistula	1	0	0.098
Liver failure	1	1	0.228
Bleeding	1	0	0.098

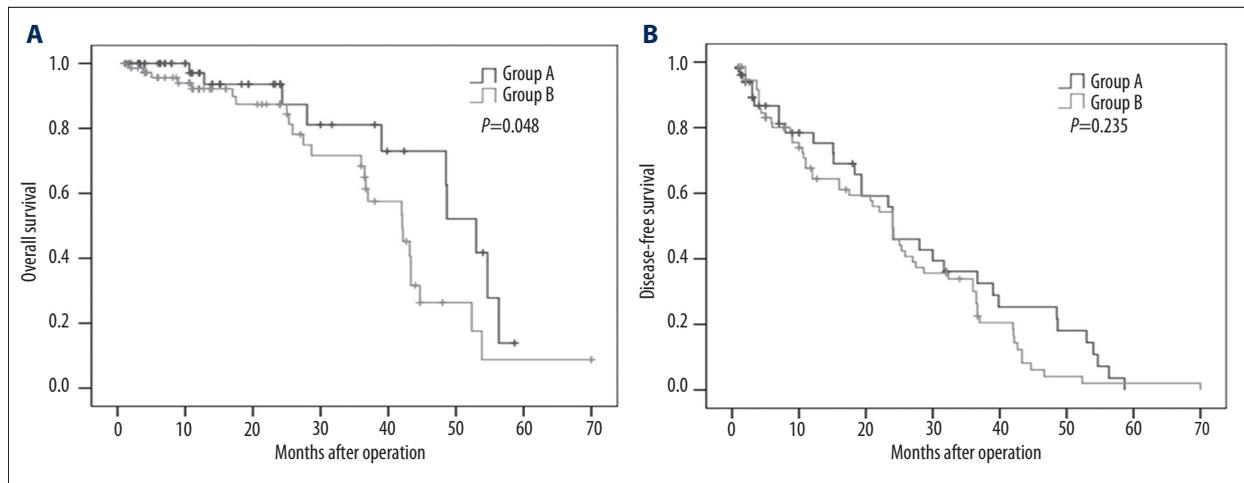


Figure 1. (A) Cumulative overall survival curves of HCC patients according to type of BMI (group A, BMI <25 vs. group B, BMI ≥25). (B) Cumulative disease-free survival curves of HCC patients according to the type of BMI (group A, BMI <25 vs. group B, BMI ≥25).

6%, respectively. Group C had significant better overall survival and disease-free survival than group D ($P=0.028$, $P=0.048$).

Discussion

There are many reports about the relationship between BMI, the size of waistline, and cancer risk [7–14]. Research conducted by the Cancer Council of Victoria, Australia shows that a waist measurement of over 100 cm for men and over 85 cm for women can significantly increase the risk of cancer including breast, bowel, and aggressive prostate cancer. However, there were few reports about the relationship between BMI,

waistline, and HCC. The high HCC rates in China are largely due to the prevalence of chronic hepatitis B virus infection. However, with the increase in prevalence of obesity, NAFLD, which can progress to cirrhosis and subsequently to the development of HCC, is now recognized as one of the most common liver diseases in China. Although many reports had affirmed that patient with higher BMI tend to show a higher incidence of liver cirrhosis, there are few reports about the relationship between the BMI and the surgical outcome of hepatectomy for HCC [15–17]. Regarding the relationship between BMI, waistline, and obesity, we hypothesized that waistline might be related to surgical outcome of hepatectomy for HCC, as well.

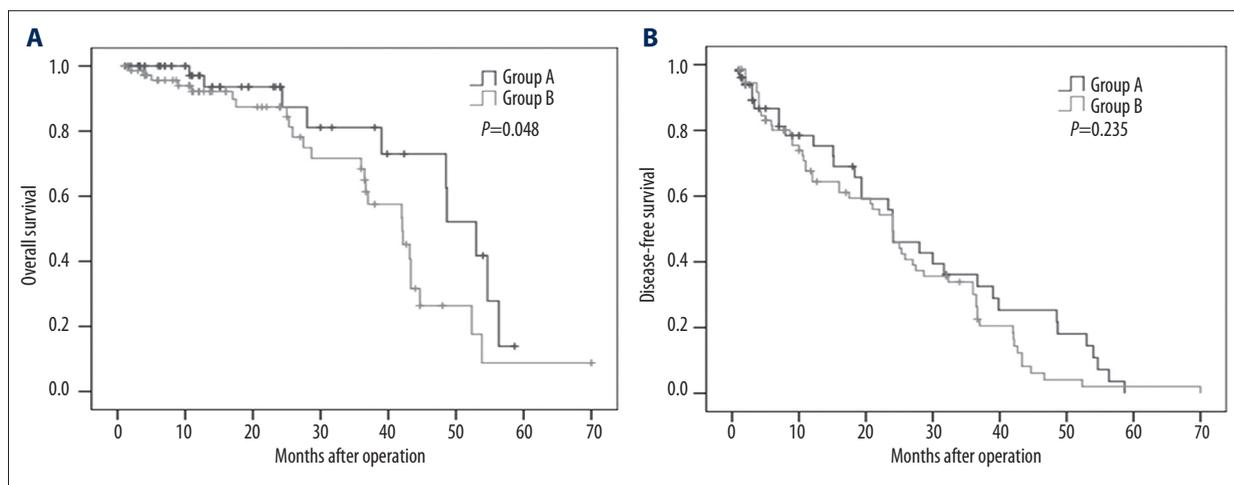


Figure 2. (A) Cumulative overall survival curves of HCC patients according to type of waistline (group C, waistline <90 cm in males or waistline <80 cm in females; group D, waistline ≥90 cm in males or waistline ≥80 cm in females). (B) Cumulative disease-free survival curves of HCC patients according to type of waistline (group C, waistline <90 cm in males or waistline <80 cm in females; group D, waistline ≥90 cm in males or waistline ≥80 cm in females).

In this study, there were no significant differences in postoperative complication rate and postoperative death between group A and group B. However, pulmonary infection (13.3%) showed a significant difference between the 2 groups ($P=0.017$). The observation that the obese patients had more pulmonary infection after hepatectomy for HCC can be explained by the fact that obesity can reduce pulmonary function through diminishing exercise capacity and lung volume, and increasing the resistance of breathing. Vascular invasion, waistline, and BMI are the independent prognostic factors for long-term survival. Group C had better overall and disease-free survival than group D, and group A had the better overall survival than group B. This result showed that BMI and waistline are both independent prognostic factors for long-term survival. Waistline may be more important than BMI in predicting the prognosis of HCC after hepatectomy. This may be attributed to the better representativeness of waistline in abdominal obesity.

Obesity, which can lead to NAFLD and finally progress to cirrhosis, is thought to account for the majority of HCC [18–21].

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With the increase in prevalence of obesity, NAFLD is now recognized as one of the most common liver diseases in China. We recommend that individuals whose BMI or waistline exceeds normal limits should cultivate a healthy lifestyle, such as eating foods that help to lose weight, regular physical exercise, and getting enough sleep.

Conclusions

In conclusion, overweight and obesity have been shown to be significant predictors of an adverse long-time survival after hepatectomy for HCC. Waistline is more important than BMI in predicting the disease-free survival of HCC after hepatectomy.

Conflict of interest

Xiyu Liu and Jiangfeng Xu have no conflicts of interest.

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