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ORIGINAL ARTICLE

Case Control Study

Synchronous splenectomy and hepatectomy for patients with hepatocellular carcinoma and hypersplenism: A case-control study

Xiao-Yun Zhang, Chuan Li, Tian-Fu Wen, Lu-Nan Yan, Bo Li, Jia-Yin Yang, Wen-Tao Wang, Li Jiang

Xiao-Yun Zhang, Chuan Li, Tian-Fu Wen, Lu-Nan Yan, Bo Li, Jia-Yin Yang, Wen-Tao Wang, Li Jiang, Department of Liver Surgery and Liver Transplantation Centre, West China Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China

Author contributions: Zhang XY and Wen TF proposed the study; Zhang XY, Li C, and Jiang L performed the research; Zhang XY, Li C, and Jiang L collected and analyzed the data; Zhang XY wrote the first draft; Wen TF reviewed the paper; all authors contributed to the design and interpretation of the study and to the revision of the manuscript.

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Correspondence to: Tian-Fu Wen, Professor, Department of Liver Surgery and Liver Transplantation Centre, West China Hospital of Sichuan University, No. 37 Guoxuexiang, Chengdu 610041, Sichuan Province, China. cdwentianfu@sohu.com
Telephone: +86-28-85422871
Fax: +86-28-85422396

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Abstract

AIM: To investigate whether the use of synchronous hepatectomy and splenectomy (HS) is more effective than hepatectomy alone (HA) for patients with hepatocellular carcinoma (HCC) and hypersplenism.

METHODS: From January 2007 to March 2013, 84 consecutive patients with HCC and hypersplenism who underwent synchronous hepatectomy and splenectomy in our center were compared with 84 well-matched patients from a pool of 268 patients who underwent hepatectomy alone. The short-term and long-term outcomes of the two groups were analyzed and compared.

RESULTS: The mean time to recurrence was 21.11 ± 12.04 mo in the HS group and 11.23 ± 8.73 mo in the HA group, and these values were significantly different (P = 0.001). The 1-, 3-, 5-, and 7-year disease-free survival rates for the patients in the HS group and the HA group were 86.7%, 70.9%, 52.7%, and 45.9% and 88.1%, 59.4%, 43.3%, and 39.5%, respectively (P = 0.008). Platelet and white blood cell counts in the HS group were significantly increased compared with the HA group one day, one week, one month and one year postoperatively (P < 0.001). Splenectomy and micro-vascular invasion were significant independent prognostic factors for disease-free survival. Gender, tumor number, and recurrence were independent prognostic factors for overall survival.

CONCLUSION: Synchronous hepatectomy and hepatectomy potentially improves disease-free survival rates and alleviates hypersplenism without increasing the surgical risks for patients with HCC and hypersplenism.

Key words: Hepatocellular carcinoma; Hypersplenism; Splenectomy; Hepatectomy; Case-control study

Core tip: The optimal approach for treating patients suffering from hepatocellular carcinoma (HCC) and hypersplenism is not well established. In the present study, synchronous hepatectomy and hepatectomy improved disease-free survival rates and alleviated hypersplenism without increasing the surgical risk for patients with HCC and hypersplenism.

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INTRODUCTION

Hypersplenism, secondary to portal hypertension, is commonly associated with hepatocellular carcinoma (HCC) in cirrhotic patients, resulting in anemia, leucopenia, and thrombocytopenia[1-3]. Given the poor preoperative situation, increased surgical risks and poor long-term survival, hypersplenism is considered a contraindication for HCC patients undergoing liver resection[4-6]. The guidelines of the American Association for the Study of Liver Disease recommended that splenectomy be performed in cirrhotic patients with preserved liver function[7]. However, splenic immune function decreases with the development of HCC[8]. Nomura *et al*[9] reported that splenectomy improved liver fibrosis and led to beneficial immunological changes in cirrhotic patients with hepatitis, and splenectomy was also suggested to improve antitumor responses. In addition, splenectomy is advocated as an effective treatment for hypersplenism and portal hypertension, as this procedure improves low white blood cell (WBC) and platelet counts and reduce portal vein pressure[1,10,11]. The selection criteria and surgical techniques have been refined, and the outcome of patients undergoing liver resection has improved[12-14], with 5-year survival rates after resection reported to exceed 50%[7,15-18]. However, the best method for treating patients suffering from HCC and hypersplenism is currently not well established.

We carefully performed synchronous hepatectomy and splenectomy (HS) in patients with HCC and hypersplenism with preserved liver function. The aim of this case-control study was to investigate whether the use of synchronous hepatectomy and splenectomy was better than hepatectomy alone (HA) for patients with HCC and hypersplenism.

Table 1 Demographic data of the hepatectomy and splenectomy group and the hepatectomy alone group

Variable	HS group	HA group	*P* value
Number of patients (*n*)	84	84	
Age (yr)	49.32 ± 10.485	51.01 ± 10.830	0.306
Gender (M/F)	69:15	69:15	1.000
HBsAg (positive/negative)	71:13	72:12	0.828
AFP (ng/mL)			0.633
≤ 400	54	51	
> 400	30	33	
White blood cell count (10^9/L)	3.96 ± 4.11	4.60 ± 4.41	0.332
Platelet count (10^9/L)	61.43 ± 42.113	68.93 ± 17.677	0.134
Splenomegaly (mild/moderate/severe)	12:46:36	14:53:27	0.380
Chlid-Pugh class (A)	84	84	
Number of tumors			
Single	11	11	1.000
Multiple	73	73	
Diameter of tumor (cm)			
Mean	4.18 ± 2.134	4.26 ± 1.996	0.809
≤ 5	13	18	0.320
> 5	71	66	
Micro-vascular invasion			
Yes	20	22	0.722
No	64	62	

HS: Hepatectomy and splenectomy; HA: Hepatectomy alone; AFP: Alpha-fetoprotein; HBsAg: Hepatitis B surface antigen.

MATERIALS AND METHODS

Case-control study

From January 2007 to March 2013, 84 consecutive patients with HCC and hypersplenism who underwent hepatectomy and splenectomy (the HS group) in the Department of Liver Surgery and Liver Transplantation Center of the West China Hospital of Sichuan University were retrospectively enrolled.

The HA group consisted of 84 patients selected from a pool of 268 patients who underwent HA for HCC and hypersplenism during the same period and met the selection criteria for hepatectomy and splenectomy. The cases and controls were well matched at a 1:1 ratio between the HS group and the HA group for the following variables: age, gender, hepatitis B surface antigen (HBsAg), alpha-fetoprotein (AFP), WBC and platelet (PLT) counts, splenomegaly, number of tumors, tumor size and micro-vascular invasion (MVI). To reduce bias, contemporary case controls were selected in a consecutive manner, and patients who received splenectomy after primary hepatectomy were excluded from the case-control study. The mean duration of follow-up was 35.87 ± 16.16 mo in the HS group and 33.45 ± 17.94 mo in the HA group. All of the enrolled patients were categorized as having Child-Pugh A liver function. The demographic data of the two patient groups are presented in Table 1.

The following data were collected for all cases and controls: length of hospital stay, follow-up time, minor and major complications (Dindo *et al*[19] classification

Table 2 Other clinical data and complication classification of the two groups

Variable	HS group (n = 84)	HA group (n = 84)	P value
Hospital stays (d)	9.71 ± 3.514	9.57 ± 5.267	0.899
Type of resection[1] (major/minor)	20:64	32:52	0.066
Intraoperative bleeding (mL)	553.57 ± 281.316	498.21 ± 220.094	0.157
Transfusion (Y/N)	11/73	8/76	0.627
Recurrence	35	48	0.045
Time to recurrence (mo)			
Mean time	21.11 ± 12.04	11.23 ± 8.73	0.001
≤ 12 mo	8	31	< 0.001
> 12 mo	27	17	
Follow-up time (mo)	35.87 ± 16.16	33.45 ± 17.94	0.360
Upper gastrointestinal hemorrhage after operation	4	7	0.349

[1]Major resection = Resection of three or more segments; Minor resection = Resection of two or fewer segments. HS: Hepatectomy and splenectomy; HA: Hepatectomy alone.

of surgical complications), type of liver resection (major *vs* minor), intraoperative bleeding, number of transfusions and time to recurrence. Data regarding total bilirubin (TBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and WBC and PLT counts were collected one day, one week, one month, and one year after the operation. The short- and long-term outcomes of the two groups were analyzed and compared.

All study subjects were informed of the benefits and risks of surgery in detail. Written informed consent for patient information to be stored in the hospital database and used for research was obtained from all patients.

Indications for splenectomy

Hypersplenism was defined as: (1) the portal vein greater than or equal to 1.0 cm in diameter; (2) the presence of hepatic cirrhosis and splenic thickness greater than or equal to 4.0 cm, as measured by radiographic examination; and (3) PLT and WBC counts less than 80 × 10^9/L and 3.0 × 10^9/L, respectively, obtained the week prior to surgery. Patients who suffered from splenomegaly with hypersplenism and/or splenomegaly that was classified as greater than class Ⅰ (spleen enlarged beyond left subcostal margin and palpable) were treated by splenectomy.

Patient follow-up

All of the patients received follow-up monitoring 1 mo after the operation, every 3 mo thereafter during the first 3 years and then every 6 mo in subsequent years. All enrolled patients received regular follow-up monitoring until death or termination of the study. Disease status was assessed according to serum liver biochemistries, AFP levels, hepatitis B virus (HBV)-DNA levels and radiological examination. One or two types of radiological examination, such as ultrasound, contrast-enhanced ultrasound, contrast-enhanced computed tomography (CT), and magnetic resonance imaging, were chosen based on the specific situation. Tumor recurrence was diagnosed based on the identification of a new lesion in at least two radiological examinations and increased AFP levels. The final follow-up visit occurred at the end of July 2014, unless the patient had died prior to that time. The overall median follow-up time was 33 mo (5-86 mo).

Statistical analysis

Continuous variables are expressed as mean ± standard deviation and were compared between groups using the t-test or Mann-Whitney U test for variables with an abnormal distribution. Categorical data were compared using the χ^2 test or Fisher's exact test. The overall survival rates were analyzed using the Kaplan-Meier method, and the differences were analyzed using the log-rank test. The Cox proportional hazard model was used for univariate and multivariate analyses of prognostic factors after surgery. Two-tailed P values ≤ 0.05 were considered statistically significant. Calculations were performed using the SPSS package (SPSS, Inc. 1989-1995, Chicago, IL).

RESULTS

According to the case-match design, age, gender, HBsAg, AFP, WBC and PLT counts, splenomegaly, tumor number, tumor size and MVI were similar between the two groups of patients (Table 1). A total of 33 patients died in the HA group, whereas 26 patients died in the HS group. The length of hospital stay, follow-up time, type of liver resection (major *vs* minor), intraoperative bleeding, and number of transfusions during the perioperative period did not significantly differ between the two groups (Table 2). The mean time to recurrence was 21.11 ± 12.04 mo in the HS group and 11.23 ± 8.73 mo in the HA group, and these values were significantly different (P = 0.001). Subgroup analyses indicated that 8 of 35 patients suffered early recurrence (time to recurrence less than 12 mo) in the HA group, whereas 31 of 48 patients in the HA group experienced early recurrence (P < 0.001).

Surgical complications

No treatment-related mortality was noted in either group (Table 3). Complications above grade II were defined as severe complications and were analyzed. In the HS group, two patients developed pleural effusion and received pleurocentesis. In addition, two patients were diagnosed with intra-abdominal bleeding and underwent re-laparotomy. As a result of hypotension and shock, two patients were resuscitated and required ICU management. In the HA group, one patient de-

Table 3 Surgical complications classified by Clavien classification for the two groups

Clavien classification	HS group	HA group	*P* value
Grade Ⅰ (fever/pain/vomit/ wound infection/ ascites/ hypokalemia)	21 (9/4/2/1/4/1)	22 (5/4/5/1/4/3)	
Grade Ⅱ (transfusion/infection/ coagulopathy/liver failure)	6 (5/1/0/0)	10 (2/5/2/1)	
Grade Ⅲa	2[1]	1[4]	
Grade Ⅲb	2[2]	0	
Grade Ⅵ	2[3]	3[5]	
Grade Ⅴ	-	-	
Total	33	36	0.532

[1]Two patients had pleural effusion and received pleurocentesis; [2]Two patients were diagnosed with intra-abdominal bleeding and underwent re-laparotomy; [3]Two patients were resuscitated and needed ICU management due to the hypotension and shock; [4]One patient had pleural effusion and received pleurocentesis; [5]Two patients suffered type Ⅰ respiratory failure and 1 patient suffered hypotension and shock, all of whom needed ICU management. HS: Hepatectomy and splenectomy; HA: Hepatectomy alone.

veloped pleural effusion and received pleurocentesis. Two patients suffered type Ⅰ respiratory failure, and one patient suffered hypotension and shock; all of these conditions required ICU management. However, no significant difference in the incidence rate or classification of complications was noted between the two groups (P = 0.532).

Survival rate

Disease-free survival rate: The 1-, 3-, 5-, and 7-year disease-free survival rates for patients in the HS group and HA group were 86.7%, 70.9%, 52.7%, and 45.9% and 88.1%, 59.4%, 43.3%, and 39.5%, respectively. Disease-free survival was enhanced in the HS group compared with the HA group (P = 0.008; Figure 1).

Overall survival rate: The 1-, 3-, 5-, and 7-year overall survival rates for patients in the HS group and HA group were 90.4%, 77.9%, 65.9%, and 45.2% and 85.7%, 70.0%, 58.3%, and 54.7%, respectively. No significant difference in overall survival was noted between the groups (P = 0.187) (Figure 2).

Laboratory tests after surgery

Total bilirubin, ALT, AST, and PLT and WBC counts were similar in both groups prior to surgery (Table 4). After surgery, the PLT and WBC counts in the HS group were significantly increased compared with the HA group (P < 0.001) (Figure 3A and B). The levels of TBIL and ALT were significantly increased in the HA group compared with the HS group on postoperative day one (P < 0.05) but then decreased to levels similar to those observed in the HS group at one week, one month and one year after the operation (Figure 3C and D). In addition,

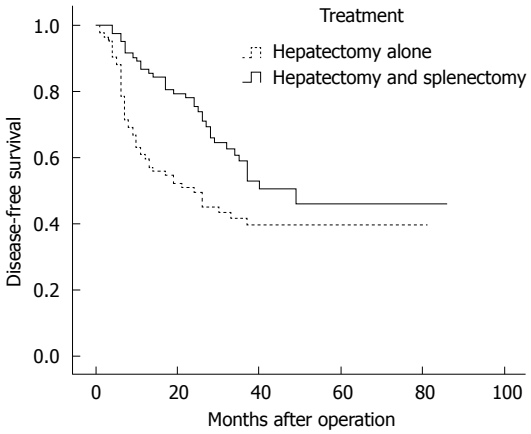

Figure 1 Disease-free survival rates of patients in the two groups. The 1-, 3-, 5-, and 7-year disease-free survival rates for the hepatectomy and splenectomy group were 86.7%, 70.9%, 52.7%, and 45.9%, respectively. The 1-, 3-, 5-, and 7-year disease-free survival rates for the hepatectomy alone group were 88.1%, 59.4%, 43.3%, and 39.5%, respectively (P = 0.008).

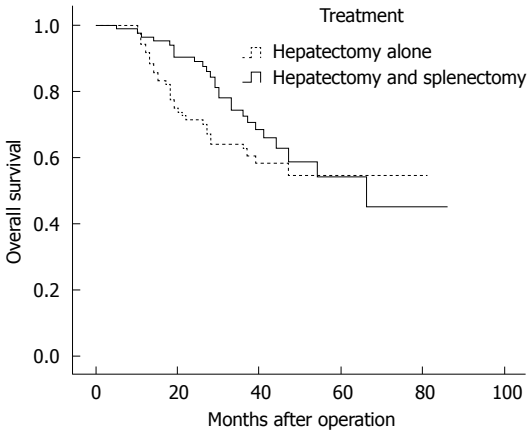

Figure 2 Overall survival rates of patients in the two groups. The 1-, 3-, 5-, and 7-year overall survival rates for the hepatectomy and splenectomy group were 90.4%, 77.9%, 65.9%, and 45.2%, respectively. The 1-, 3-, 5-, and 7-year overall survival rates for the hepatectomy alone group were 85.7%, 70.0%, 58.3%, and 54.7%, respectively (P = 0.187).

the serum AST levels did not differ between the two groups in the short-term or long-term period after surgery (P > 0.05).

Prognostic factors for patients with HCC and hypersplenism

Disease-free survival: Splenectomy (HR = 0.531; 95%CI: 0.341-0.828; P = 0.005) and MVI (HR = 2.642, 95%CI: 1.685-4.143; P < 0.001) were identified as significant independent prognostic factors for disease-free survival using univariate and multivariate analyses (Table 5).

Overall survival: Univariate analysis indicated that the following four variables were statistically significant prognostic factors associated with overall survival in patients with HCC and hypersplenism: gender (female, P = 0.020), tumor number (multiple, P = 0.041),

Table 4 Laboratory tests of the two groups after surgery

Variable	Pre-operation			1 d			1 wk			1 mo			1 yr		
	HS	HA	*P* value	HS	HA	*P* value	HS	HA	*P* value	HS	HA	*P* value	HS	HA	*P* value
TBIL (μmol/L)	17.94 ± 7.34	16.62 ± 6.63	0.415	22.34 ± 8.52	32.72 ± 27.14	0.026	24.04 ± 10.90	34.06 ± 48.89	0.216	15.12 ± 5.28	15.87 ± 6.70	0.858	17.20 ± 6.21	18.61 ± 5.82	0.314
ALT (IU/L)	35.90 ± 16.89	39.24 ± 14,54	0.519	213.85 ± 187.27	348.00 ± 342.49	0.036	112.00 ± 101.69	169.57 ± 154.49	0.058	43.49 ± 23.78	49.41 ± 21.62	0.860	39.82 ± 17.85	41.11 ± 34.53	0.838
AST (IU/L)	39.92 ± 15.69	47.16 ± 27.63	0.162	244.49 ± 186.49	321.81 ± 314.90	0.194	80.64 ± 77.53	64.19 ± 37.23	0.246	49.41 ± 21.62	44.22 ± 22.31	0.306	47.69 ± 27.73	48.00 ± 48.75	0.973
PLT count (10^9/L)	61.43 ± 42.11	68.93 ± 17.68	0.134	98.54 ± 33.27	67.11 ± 21.67	< 0.001	230.95 ± 114.95	74.65 ± 26.05	< 0.001	214.18 ± 102.03	73.24 ± 24.12	< 0.001	199.97 ± 58.19	68.08 ± 36.52	< 0.001
WBC count (10^9/L)	3.96 ± 4.11	4.60 ± 4.41	0.332	16.30 ± 5.38	11.79 ± 4.07	< 0.001	10.93 ± 4.27	6.14 ± 2.74	< 0.001	6.48 ± 1.71	4.25 ± 1.41	< 0.001	5.96 ± 1.46	4.48 ± 2.02	< 0.001

Both PLT and WBC counts in the HS group were alleviated and were significantly higher when compared to those in the HA group at one day, one week, one month and one year postoperatively ($P < 0.001$) (Figure 3A and B). While levels of the TBIL and ALT were much higher in the HA group than in the HS group on postoperative day one ($P < 0.05$), and then descended as similar as the HS group (Figure 3C and D). The level of AST did not differ between the two groups. TBIL: Total bilirubin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; PLT: Platelet; WBC: White blood cell.

tumor size (> 5 cm, $P = 0.027$) and recurrence ($P < 0.001$). Furthermore, based on the multivariate analysis, gender (HR = 0.774; 95%CI: 1.164-4.041; $P = 0.015$), tumor number (HR = 0.801; 95%CI: 1.071-4.633; $P = 0.032$), and recurrence (HR = 2.344; 95%CI: 4.961-21.882; $P < 0.001$) were independent prognostic factors for long-term survival in patients with HCC and hypersplenism (Table 6).

DISCUSSION

Perioperative bleeding control and postoperative liver failure are the major concerns for cirrhotic patients with HCC and hypersplenism[4,5,7]. However, splenectomy has been suggested as a method to overcome these problems, as this procedure can reduce serum bilirubin levels and improve liver function[1,11]. In addition, PLT counts increase immediately after splenectomy, thereby potentially reducing intraoperative bleeding and surgical risk[20,21]. In the present case-control study, TBIL and ALT levels were reduced at one day and one week postoperatively in patients undergoing synchronous hepatectomy and splenectomy compared to those treated by hepatectomy alone. In addition, intraoperative bleeding and severe surgical complications were similar between the two groups. Furthermore, the disease-free survival was significantly increased in the HS group compared with the HA group, suggesting that synchronous hepatectomy and splenectomy are safe and beneficial for patients with HCC and hypersplenism.

The immunophysiology of the spleen in cirrhotic patients and the long-term outcomes of such patients after splenectomy are not fully understood. Aoe *et al*[22] reported that a large number of activated macrophages accumulated in the spleens of tumor-bearing hosts, which led to an abnormal T cell receptor-CD3 complex and suppressed the immune function of T cells. In addition, Ugel *et al*[23] recently reported that the spleen was fundamentally important for tumor-induced tolerance. Splenic CD11b+Gr-$1^{int}$$Ly6^{Chi}$ cells, which are mostly composed of proliferating CCR2+ inflammatory monocytes with myeloid progenitor features, expand in the marginal zone of the spleen, where these cells alter the normal tissue cytoarchitecture and cross-present tumor antigens to memory CD8+ T cells, resulting in tolerization[23]. Accordingly, splenectomy was shown to restore lymphocyte function and induce tumor regression when coupled with immunotherapy. Shimada *et al*[11] and Karakantza *et al*[24] reported that splenectomy increased the number of natural killer (NK) cells. In addition, the immune response against cancer is altered after splenectomy due to the modulation of CD4+ and CD8+ T cells[9,25,26]. Splenectomy results in a reduction of transforming growth factor (TGF)-β1, which is produced and secreted by the spleen, thereby significantly improving liver regeneration and ameliorating liver cirrhosis[27-29]. Thus, we hypothesized that splenectomy may play a prophylactic role against HCC recurrence after liver resection, and our results showed that disease-free survival and the time interval before recurrence were enhanced in the HS group compared with the HA group, which is consistent with a previous study[26].

Interestingly, synchronous hepatectomy and splenectomy decreased tumor recurrence and prolonged the interval to recurrence; however, this technique was not beneficial to the overall survival of patients with HCC and hypersplenism. The reduction of TGF-β levels after splenectomy was shown to lead to decreased recruitment of T regulatory (Treg) cells *via* the TGF-β-miRNA-34a-CCL22 pathway[30,31], which may reduce the ability of HCC cells to evade immune defenses and inhibit tumor

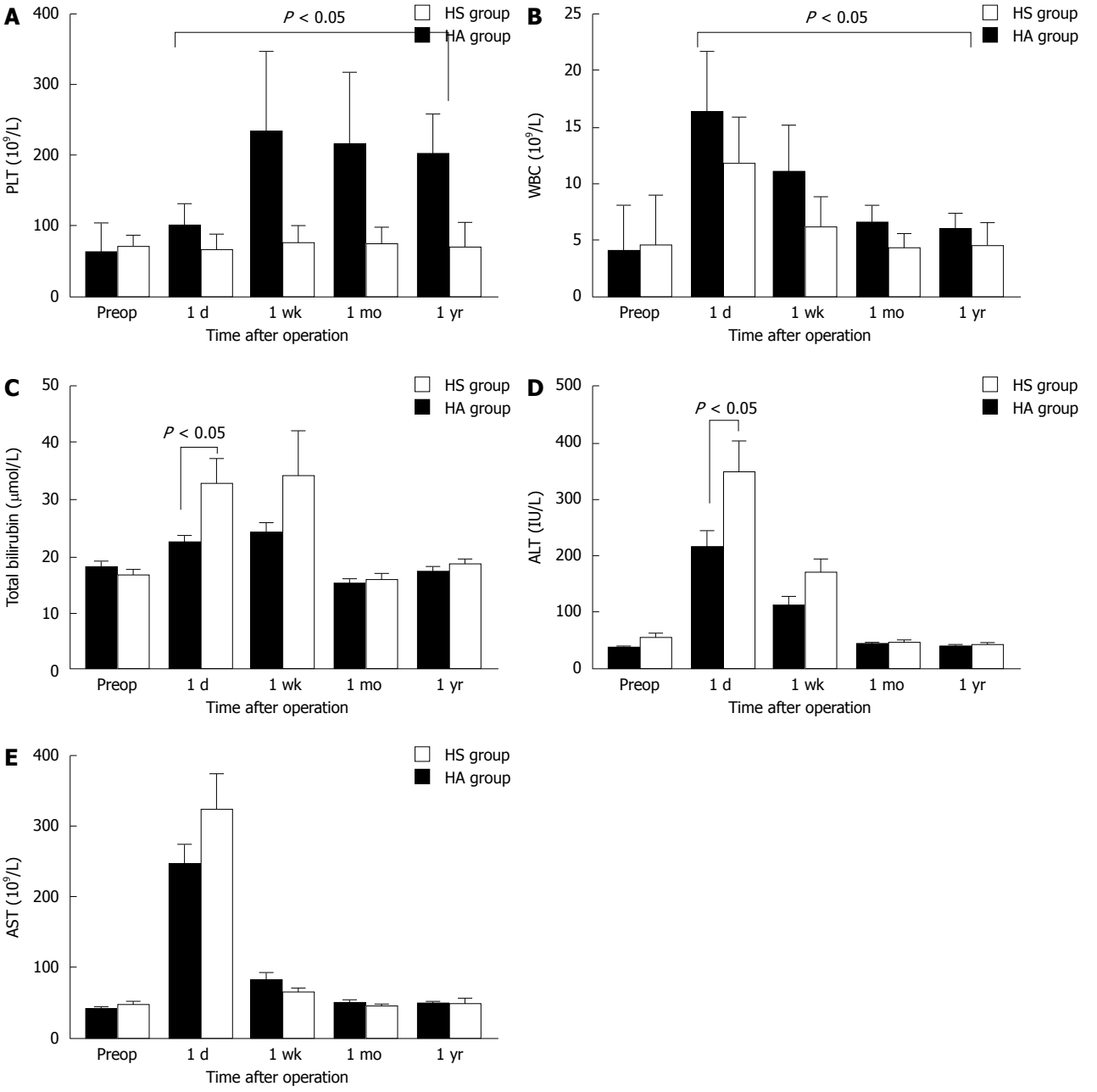

Figure 3 Changes in laboratory test results between the two groups. The platelet and white blood cell counts in the HS group were significantly increased compared with the HA group one day, one week, one month and one year postoperatively ($P < 0.001$) (A and B); Total bilirubin and ALT levels were significantly increased in the HA group compared with the HS group on postoperative day one ($P < 0.05$) and then decreased to levels similar to those observed in the HS group (C and D); E: The AST levels did not differ between the two groups. HS: Hepatectomy and splenectomy; HA: Hepatectomy alone; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; PLT: Platelet; WBC: White blood cell.

metastasis. Intricate immunosuppressive mechanisms, such as abnormal T cell receptor-CD3 complex[22], tumor-induced tolerance[23], suppression of NK cells[11,24], and impaired T cell function, may also be altered by splenectomy, thereby temporarily inducing tumor regression. However, sustained hepatitis viral infection results in inflammation and inflammatory microenvironments that promote fibrosis, cirrhosis and even permanent oncogenesis. As demonstrated in the present study, most patients were characterized as hepatitis b antigen-positive; thus, the outcomes of the case-control groups were not significantly different ($P = 0.187$).

In addition, numerous reports suggest that patients can significantly benefit from splenectomy. Hepatic resection increases portal hypertension, which is potentially associated with upper gastrointestinal hemorrhage[32]. Splenectomy reduces 20%-30% of the portal vein inflow, thereby greatly decreasing portal hypertension[33,34]. A total of four patients in the HS group experienced an episode of upper gastrointestinal hemorrhage after liver resection, whereas seven patients in the HA group experienced hemorrhage. In addition, WBC and PLT counts were significantly

Table 5 Univariate and multivariate analyses of prognostic factors for disease-free survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Splenectomy	0.498 (0.314-0.792)	0.003	0.531 (0.341-0.828)	0.005
Gender, F	0.873 (0.476-1.601)	0.661		
Age, > 60 yr	0.836 (0.395-1.769)	0.639		
HBsAg, positive	1.634 (0.716-3.727)	0.243		
AFP, > 400 ng/mL	1.386 (0.881-2.180)	0.158		
Platelet count	0.994 (0.985-1.003)	0.221		
White blood cell count	1.037 (0.993-1.083)	0.1		
Tumor number, multiple	1.668 (0.862-3.226)	0.129		
Tumor size, > 5 cm	0.785 (0.446-1.381)	0.401		
Micro-vascular invasion	2.766 (1.700-4.498)	<0.001	2.642 (1.685-4.143)	< 0.001

HBsAg: Hepatitis B surface antigen; AFP: Alpha-fetoprotein.

Table 6 Univariate and multivariate analyses of prognostic factors for overall survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Splenectomy	0.862 (0.497-1.492)	0.595		
Gender, F	0.466 (1.125-4.083)	0.020	0.774 (1.164-4.041)	0.015
Age, > 60 yr	0.876 (0.384-1.998)	0.752		
HBsAg, positive	0.552 (0.259-1.176)	0.124		
AFP, > 400 ng/mL	0.986 (0.563-1.728)	0.962		
Platelet count	1.004 (0.995-1.013)	0.397		
White blood cell count	0.975 (0.901-1.055)	0.533		
Tumor number, multiple	2.216 (1.033-4.752)	0.041	0.801 (1.071-4.633)	0.032
Tumor size, > 5 cm	2.067 (1.087-3.930)	0.027	0.572 (0.991-3.169)	0.054
Micro-vascular invasion	0.624 (0.329-1.182)	0.148		
Recurrence	14.376 (6.233-33.160)	< 0.001	2.344 (4.961-21.882)	< 0.001

HBsAg: Hepatitis B surface antigen; AFP: Alpha-fetoprotein.

elevated after splenectomy. Thus, it was possible to administer adjuvant chemotherapy, which may prevent HCC recurrence[26,35,36].

This study had several limitations. First, given that it was not a randomized study, selection bias may be inherent to the study. To reduce this bias, we selected contemporary case controls in a consecutive manner and excluded patients who received splenectomy after primary hepatectomy. Second, the number of subjects was relatively small. A large randomized control study is thus needed to confirm the role of HS in improving disease-free survival for patients with HCC and hypersplenism.

In conclusion, our results suggest that synchronous hepatectomy and hepatectomy may improve disease-free survival rates and alleviate hypersplenism without an increased surgical risk for patients with HCC and hypersplenism.

COMMENTS

Background

Given its poor preoperative characteristics, increased surgical risks and poor long-term survival, hypersplenism is considered a contraindication for hepatocellular carcinoma (HCC) patients undergoing liver resection. Moreover, the optimal method to treat patients suffering from HCC and hypersplenism is not well established. Therefore, the authors conducted this case-control study to investigate whether the use of synchronous hepatectomy and splenectomy was better than hepatectomy alone for patients with HCC and hypersplenism.

Research frontiers

The immunophysiology of the spleen in cirrhotic patients has not been fully characterized. Splenectomy potentially restores lymphocyte function and induces tumor regression when coupled with immunotherapy.

Innovations and breakthroughs

Synchronous splenectomy may play a prophylactic role against hepatocellular carcinoma recurrence after liver resection.

Applications

The use of synchronous hepatectomy and splenectomy may improve disease-free survival and alleviate hypersplenism without increasing the surgical risk for patients with HCC and hypersplenism.

Terminology

The immunosuppressive mechanisms of HCC, including defective antigen presentation, tumor-induced tolerance, impaired $CD4^+$ T cell function, suppression of natural killer cells, recruitment of immunosuppressive myeloid and lymphoid cell populations and the up-regulation of immune checkpoint pathways, are intricate and further interfere with the development of a meaningful anti-tumor response.

Peer review

This is an interesting study that aims to determine the role of splenectomy and hepatectomy for patients with hepatocellular carcinoma and hypersplenism.

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