P.O.Box 2345, Beijing 100023,China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

World J Gastroenterol 2003;9(8):1702-1706
World Journal of Gastroenterology
 ISSN 1007-9327

• LIVER CANCER •

Role of preoperative selective portal vein embolization in two-step curative hepatectomy for hepatocellular carcinoma

Wu Ji, Jie-Shou Li, Ling-Tang Li, Wu-Hong Liu, Kuan-Sheng Ma, Xiang-Tian Wang, Zhen-Ping He, Jia-Hong Dong

Wu Ji, Jie-Shou Li, Ling-Tang Li, Research Institute of General Surgery, Nanjing General Hospital of Nanjing PLA Command Area, Nanjing 210002, Jiangsu Province, China
Wu Ji, Wu-Hong Liu, Xiang-Tian Wang, Department of General Surgery, Kunming General Hospital of Chengdu PLA Command Area, Kunming 650032, Yunnan Province, China
Kuan-Sheng Ma, Zhen-Ping He, Jia-Hong Dong, Hepatobiliary Surgery Center, Southwest Hospital, Third Military Medical University, Chongqing 400038, China
Correspondence to: Wu Ji, MD, Institute of General Surgery, Nanjing General Hospital of Nanjing PLA Command Area, 305 Eastern Zhongshan Road, Nanjing, 210002, Jiangsu Province, China. jiwusky@sohu.com
Telephone: +86-25-4826808 Ext 58007 **Fax:** +86-25-4820160
Received: 2002-11-06 **Accepted:** 2002-12-07

Abstract

AIM: To determine the feasibility and role of ultrasound-guided preoperative selective portal vein embolization (POSPVE) in the two-step hepatectomy of patients with advanced primary hepatocellular carcinoma (HCC).

METHODS: Fifty patients with advanced HCC who were not suitable for curative hepatectomy were treated by ultrasound-guided percutaneous transhepatic POSPVE with fine needles. The successful rate, side effects and complications of POSPVE, changes of hepatic lobe volume and two-step curative hepatectomy rate after POSPVE were observed.

RESULTS: POSPVE was successfully performed in 47 (94.0 %) patients. In patients whose right portal vein branches were embolized, their right hepatic volume decreased and left hepatic volume increased gradually. The ratio of right hepatic volume to total hepatic volume decreased from 62.4 % before POSPVE to 60.5 %, 57.2 % and 52.8 % after 1, 2 and 3 weeks respectively. The side effects included different degree of pain in liver area (38 cases), slight fever (27 cases), nausea and vomiting (9 cases). The level of aspartate alanine transaminase (AST), alanine transaminase (ALT) and total bilirubin (TBIL) increased after POSPVE, but returned to preoperative level in 1 week. After 2-4 weeks, two-step curative hepatectomy for HCC was successfully performed on 23 (52.3 %) patients. There were no such severe complications as ectopic embolization, local hemorrhage and bile leakage.

CONCLUSION: Ultrasound-guided percutaneous transhepatic POSPVE with fine needles is feasible and safe. It can extend the indications of curative hepatectomy of HCC, and increase the safety of hepatectomy.

Ji W, Li JS, Li LT, Liu WH, Ma KS, Wang XT, He ZP, Dong JH. Role of preoperative selective portal vein embolization in two-step curative hepatectomy for hepatocellular carcinoma. *World J Gastroenterol* 2003; 9(8): 1702-1706
http://www.wjgnet.com/1007-9327/9/1702.asp

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors of mankind. It threatens our life severely[1-5]. In China, HCC is responsible for about 130 000 deaths every year. It has ranked second of cancer mortality since 1990[6,7]. Surgical resection of the tumors is considered the only potentially curative therapy, and it is regarded as the first choice for the treatment of HCC. Many factors can affect hepatectomy, such as tumor size, location, multifocality and patients' status, hepatic function. Besides, 80 % of them are complicated with cirrhosis in China. So the extension of hepatectomy of HCC is greatly limited. Hepatectomy with less hepatic volume resected may be helpful to the safety of the operation, but this may not be a radical cure, and even lead to tumor residual. Hepatectomy with more hepatic volume resected will lead to postoperative hepatic failure, infection, hemorrhage and even death. So only 15 % to 30 % patients have a chance of receiving curative hepatectomy[8-10]. Most HCC patients are in late stages at the time of diagnosis. They are considered not suitable for operation. Researchers have proposed the concept of "two-step hepatectomy", and some progresses have been made in the past decades[11-15]. In 1986, Kinoshita *et al*[16] reported the experience of two-step hepatectomy after POSPVE. This is a completely new method. The purpose is to induce atrophy of the embolized (tumor) lobe and compensatory hypertrophy of the remnant lobe. The result is an increase of the remnant liver volume and a decreased ratio of resected volume to total liver volume. In recent years, reports of two-step hepatectomy after preoperative selective portal vein embolization (POSPVE) gradually increased[17-22]. But there are no such clinical reports in China.

In this study, based on an analysis of the feasibility and safety of ultrasound-guided percutaneous transhepatic POSPVE with fine needles in 50 HCC patients, we discussed the role of POSPVE in the two-step curative hepatectomy for moderate and advanced HCC.

MATERIALS AND METHODS

Eligibility of patients

This study involved 50 HCC patients. There were 36 males and 14 females. Forty three (86.0 %) patients were hepatitis surface antigen (HBsAg) positive, and 34 (68 %) were complicated with cirrhosis. Child-Pugh' s classification showed that 14 (28 %) patients were grade A, 33 (66 %) grade B, 3 (6 %) grade C. The diameter of space occupying lesions ranged from 8.1 to 16.3 cm, averaging 13.6 cm. The criteria of these patients included: HCC located in one side of the liver, with no confirmed portal vein thrombosis and distant metastasis. The ratio of hepatic volume to be resected to total hepatic volume was more than 50 % for those patients with cirrhosis and 60 % for those without cirrhosis. Those patients with coexisted morbidity-related diseases, poor life expectancy, multinodular or diffuse intrahepatic tumor, prothrombin activity less than 50 %, or platelet count lower than 50×10^9/L were excluded from the study.

Methods

One hundred microgram dolantin and 25 mg phenergan were

injected into the muscle before POSPVE. The liver, tumor and the portal vein branch to be embolized were carefully examined, located and confirmed by ultrasound. Local anesthesia was adopted with 2 % lidocaine transcutaneously down to liver surface. Under ultrasound guidance, we punctured percutaneously and transhepatically with a 21-gague PTC needle from the side of ultrasound head. When the needle was inserted into the portal vein branch to be embolized, the internal part of the needle was taken away, and dark red portal vein blood could be seen (Figure 1). Then embolic material was slowly injected into the portal vein. It consisted of a mixture of ethanol and iodized oil with a rate of 1:2. And 0.4 ml/kg was regarded as the standard dosage. Real-time ultrasonic scan showed that tiny spot echoes in the embolized portal vein branch appeared and diffused into the carcinoma. Intensified echoes appeared in some areas. After that, the fine needle was slowly pulled out. Flexible fabric bandage was used to cover the puncture spot. The patients inhaled oxygen after returning back to the ward. Changes of vital signs were monitored for 12 to 24 hours. They were given fluid infusion and anti-inflammation, hemorrhage prevention, liver function protection and analgesics treatments.

The successful rate of POSPVE, side effects and complications after POSPVE, changes of blood routine, liver function, and renal function were observed to evaluate the feasibility and safety of ultrasound-guided percutaneous transhepatic POSPVE with fine needles. Serial changes of hepatic lobe volume calculated with volume CT, ratio of right hepatic lobe volume to total hepatic volume, two-step curative hepatectomy rate after POSPVE were observed to evaluate the role of POSPVE in the two-step hepatectomy of HCC.

Statistical method

Quantitative variables were expressed as mean ± standard error of the mean. The statistical software SPSS10.0 was used. *P* value <0.05 was considered significant.

RESULTS

Feasibility and safety of POSPVE

Ultrasound-guided percutaneous transhepatic POSPVE with fine needles was successfully performed in 47 of 50 patients. The successful rate was 94.0 % (Figure 1). Three patients failed to finish the operation. The right portal vein branches were difficult to locate under ultrasound guidance because of the tumor compression in 2 of them, and one patient could not tolerate the irritation of embolic material. There were 44 right portal vein embolizations and 3 left portal vein embolizations. The side effects included different degree of pain in liver area (38 cases), slight fever (27 cases), nausea and vomiting (9 cases). The level of aspartate alanine transaminase (AST), alanine transaminase (ALT) and total bilirubin (TBIL) increased in 31 cases after POSPVE, but returned to preoperative level in 1 week. There were no such severe complications as ectopic embolization, local hemorrhage and bile leakage.

Role of POSPVE in two-step curative hepatectomy of HCC

In 44 patients whose right portal vein branches were embolized, the right hepatic volume decreased, the left hepatic volume increased and the ratio of right liver volume to total liver volume decreased gradually (Figures 2-3) (Table 1). Two to four weeks later, curative hepatectomies were successfully performed in 23 (52.3 %) patients (Figures 4-5). There were 6 irregular right hepatectomies, 15 regular right hepatectomies, and 2 right trisegmentectomies. All these 23 patients recovered smoothly, without any severe complications like hepatic failure, hemorrhage and infection. They were discharged 11 to 20 days after operations. The other 27 patients who could not receive curative hepatectomy after POSPVE were treated by transcatheter artery embolization (TAE) or chemotherapy, immune therapy and so on.

Table 1 Serial changes of liver volume and ratio of right hepatic lobe volume to total hepatic volume after right portal vein embolization

	Right liver volume (cm^3)	Left liver volume (cm^3)	Right liver volume / total liver volume (%)
Before POSPVE	592.4±98.5	352.2±65.2	62.4±7.6
1 week after POSPVE	571.7±104.0	378.6±127.9	60.5±9.3
2 weeks after POSPVE	547.7±118.3[a,c]	405.9±130.2[a,c]	57.2±11.2[a,c]
3 weeks after POSPVE	509.1±123.8[b,c,e]	446.1±143.5[b,d,e]	52.8±12.3[b,c,e]

[a]$P<0.05$, [b]$P<0.01$, *vs* before POSPVE; [c]$P<0.05$, [d]$P<0.01$, *vs* 1 week after POSPVE, [e]$P<0.05$, [f]$P<0.01$, *vs* 2 weeks after POSPVE.

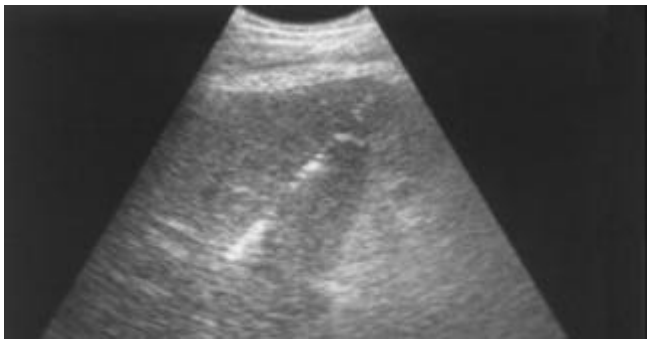

Figure 1 The fine needle was inserted into the right portal vein branch under ultrasound guidance. After embolization material was injected, tiny spot echoes appeared in the portal vein branch and diffused to the carcinoma area.

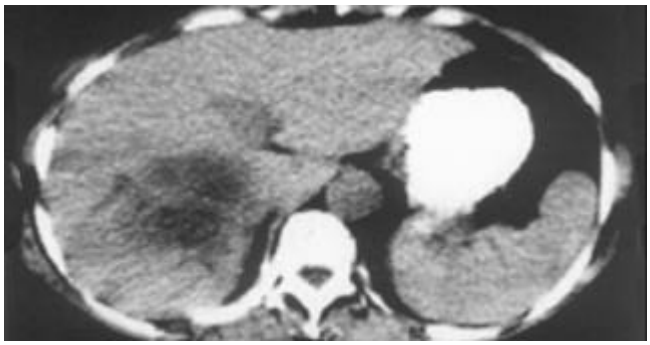

Figure 2 Before POSPVE, CT scan showed a 13.2 cm×10.8 cm HCC in the right lobe of liver. A right semihepatectomy was scheduled to perform.

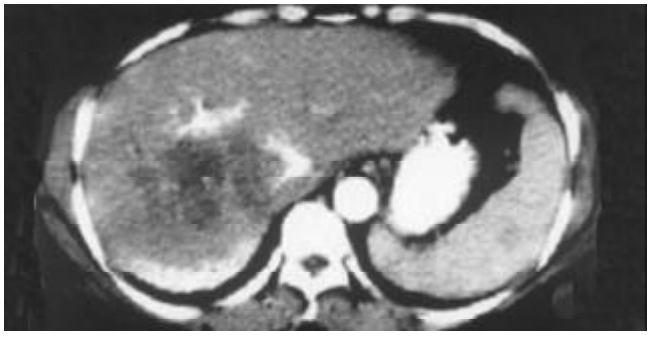

Figure 3 Three weeks after right POSPVE, CT scan showed increased volume of left lobe and decreased volume of right lobe. Iodized oil deposit still could be seen in the right portal vein branch.

Figure 4 Three weeks after right POSPVE, a right semihepatectomy was performed. In the operation, significant hypertrophy of left lobe was confirmed.

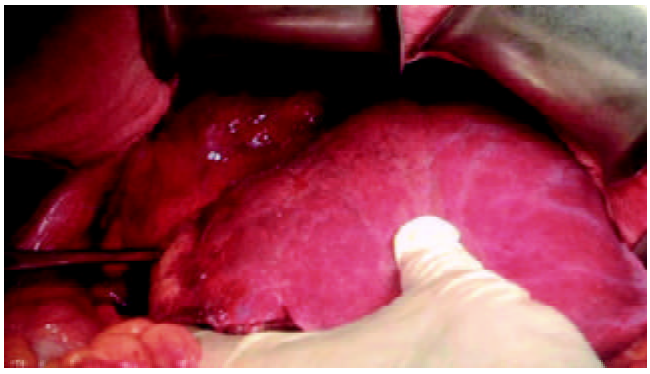

Figure 5 In the same operation, significant atrophy of right lobe and HCC could be seen. There was iodized oil deposit in the carcinoma area.

DISCUSSION

Rous and Larimore observed in 1920 that portal vein ligation in rabbit led to atrophy of the ipsilateral hepatic lobe and hypertrophy of the contralateral lobe. In 1956, Schalm confirmed it by occluding the portal vein branch. These observations provided the foundation for the study of liver regeneration after portal vein branch embolization. In 1975, Honjo found that portal vein ligation could significantly prolong the survival span of advanced HCC patients whose tumors could not be resected during operations. In 1986, Kinoshita published the first report demonstrating the efficacy of POSPVE before curative resection on primary and metastatic HCC. After that, POSPVE was gradually accepted in preparing large hepatectomy for HCC. It has been confirmed that POSPVE can extend the indication of curative hepatectomy for HCC, increase the safety of hepatectomy, and improve the long-term survival rate after the operation[23-32].

Portal vein blood supply is very important for both liver and HCC. Portal vein branch ligation or embolization results in redistribution of portal vein blood that is essential to liver regeneration. Most portal blood rich in hepatatrophic substances, such as insulin, glucagon and hepatocyte growth factor, flows toward the future remaining lobe. This leads to atrophy of the ipsilateral hepatic lobe and hypertrophy of the contralateral lobe. Harada *et al*[33] observed that POSPVE induced hepatocyte apoptosis and atrophy of the embolized lobe. Increased sinusoidal volume in this lobe may be attributable to hepatocyte deletion. Cells in the nonembolized lobe entered a highly active phase of proliferation within 2 weeks after POSPVE. Further evidences of cellular proliferation were provided by the increased nonembolized lobar volume and numerical density of hepatocyte nuclei (Nv). They concluded that the favorable role of POSPVE was attributed to a net gain of functional hepatocyte mass and early induction of hepatocyte proliferation. Shimizu *et al*[34] demonstrated that expression of proliferating cell nuclear antigen (PCNA) and mitotic index (MI) of hepatocytes in nonembolized lobe increased greatly. The amount of mitochondrial DNA-binding proteins increased 200-300 % of the preoperative level at 12 hours after ligation of left branch of the portal vein, before an increase of 390 % in mitochondrial DNA content at 24 hours, and was parallel to an increase of 240 % in mitochondrial mRNA at 12 hours. These results suggest that the energy supply for liver regeneration is achieved through enhancement of mitochondrial DNA replication as well as transcription, in which mitochondrial DNA-binding proteins probably play regulatory roles. Chijiiwa *et al*[35-37] found that the volume of nonembolized left lobe significantly increased after right POSPVE, with a significant increase in percentage of the left lobe to total liver volume. Concentrations of AMP, ADP, and ATP, and hepatic energy charge levels in the nonembolized left lobe were similar to those of the control liver. These results suggest that right POSPVE increased the volume of nonembolized left lobe, while keeping the hepatic engery charge and ATP levels similar to the control liver, thereby increasing the total amount of ATP and hepatic energy reserve of the nonembolized lobe in proportion to its volume increase at the time of surgery.

Two major techniques have been reported to access the portal vein: direct catheterization of the ileocolic vein and the percutaneous approach[38,39]. The former involves an open technique in which the ileocolic vein is cannulated at laparotomy. It is usually used when the carcinoma can not be resected during operation. This method can also be used when interventional facilities are not available for the percutaneous approach. The later can be finished under ultrasound guidance with local anesthesia. There are two major kinds of methods. One is to insert a catheter percutaneously into the portal vein branch, the other is to puncture the portal vein branch by a fine needle under ultrasound guidance. Most reports used the catheterization method. But it is technically complicated and expensive. Percutaneous approach with a fine needle is easy to perform, and patients suffer less and resume faster. But it has not been widely accepted. Its feasibility, safety and efficiency have not been discussed based on a large sample[40,41]. In this study, POSPVE with a fine needle was feasible in 47 of 50 HCC patients. The successful rate was 94.0 %. The complication rate was low, and there was no severe complication. The side effects were moderate. In 44 patients whose right portal veins were embolized, their right hepatic volume decreased and left hepatic volume increased, the ratio of hepatectomy decreased gradually. By inducing hypertrophy of the remaining liver, hepatectomies were successfully performed in 23 patients. The two-step curative hepatectomy after POSPVE was 52.3 %. All the patients recovered smoothly. It is concluded from this study that ultrasound-guided percutaneous transhepatic POSPVE with a fine needle is feasible, safe and effective. It extends the indication of curative hepatectomy for moderate and advanced HCC. This is the first report on the role of POSPVE in the treatment of HCC in China. Estimating the volume of the lobe that will remain after hepatectomy is thought to be mandatory for all patients undergoing extensive hepatic resection. If this volume is not large enough in terms of the risk of postoperative liver failure, then POSPVE is indicated. According to a criterion based on liver volumetry, POSPVE is usually indicated for patients who will undergo right trisegmentectomy, left trisegmentectomy, or right hepatectomy for cirrhosis patients. Many methods have been used to estimate the lobar volume. In this series, we used volume CT to calculate the exact volume of every lobe, and regard the ratio of hepatic volume to be resected to total hepatic

volume is more than 50 % for those patients with cirrhosis and 60 % for those without cirrhosis. The degree of hypertrophy induced in nonembolized lobe showed a large interindividual difference. It has been reported that male, diabetes mellitus and cirrhosis are negative factors, and cholestasis is a positive factor. Other factors that may influence the role of POSPVE include embolization materials and their dosage and extent[42-46]. Cyanoacrylate, lipiodol, gelatin sponge, thrombin, fibrin glue, gelfoam, and alcohol have been used as embolization materials. Their effects are controversial. We used lipidol and alcohol routinely as embolization materials throughout the study period. The functional burden placed on the liver by POSPVE using these materials was minimal and transient, as reflected in the slight elevation of AST, ALT and total bilirubin level. It was reported that the average future remaining hepatic volume increased by 28 % within 2 weeks after POSPVE. The rate of average hepatectomy decreased from 70.0 % before POSPVE to 62.2 %, and the two-step hepatectomy rate was 63.3 % to 77.4 %. But in this series, the two-step curative hepatectomy rate after POSPVE was 52.3 %. We think the main reason is that most patients in our study were male and coexisted with cirrhosis. They have been reported to be the negative regulatory factors of POSPVE. Besides, we used the method of ultrasound-guided percutaneous transhepatic POSPVE with a fine needle. It is safe, feasible and effective. The disadvantage of this method lies in that the embolization materials usually used are ethanol and iodized oil. So, it is mainly the distant branches of portal vein that are embolized. Besides, the role of ethanol is dosage dependent, while a large dosage is unbearable for most patients.

Although the concept of POSPVE appears to be well accepted and the procedure is performed ever more widely, there are a number of issues on which a general consensus has not yet been reached, such as the optimum duration between POSPVE and hepatectomy, the most suitable embolizing material and method of portal vein cannulation, the rate of technical failure and complications, and factors that accelerate or suppress the effect of POSPVE[32]. The fact that POSPVE is well tolerated might enlarge its indications in the future. POSPVE will be used not only for patients with possibly insufficient remaining liver volume after hepatectomy, but also for those whose curative operation may not be very safe.

REFERENCES

1 **Tang ZY**. Hepatocellular carcinoma-cause, treatment and metastasis. *World J Gastroenterol* 2001; **7**: 445-454
2 **Makuuchi M**, Imamura H, Sugawara Y, Takayama T. Progress in surgical treatment of hepatocellular carcinoma. *Oncology* 2002; **62**(Suppl): 74-81
3 **Fan J**, Wu ZQ, Tang ZY, Zhou J, Qiu SJ, Ma ZC, Zhou XD, Ye SL. Multimodality treatment in hepatocellular carcinoma patients with tumor thrombi in portal vein. *World J Gastroenterol* 2001; **7**: 28-32
4 **Makuuchi M**. Remodeling the surgical approach to hepatocellular carcinoma. *Hepatogastroenterology* 2002; **49**: 36-40
5 **Curley SA**, Cusack JC Jr, Tanabe KK, Stoelzing O, Ellis LM. Advances in the treatment of liver tumors. *Curr Probl Surg* 2002; **39**: 449-571
6 **Zhao WH**, Ma ZM, Zhou XR, Feng YZ, Fang BS. Prediction of recurrence and prognosis in patients with hepatocellular carcinoma after resection by use of CLIP score. *World J Gastroenterol* 2002; **8**: 237-242
7 **Qin LX**, Tang ZY. The prognostic significance of clinical and pathological features in hepatocellular carcinoma. *World J Gastroenterol* 2002; **8**: 193-199
8 **Rabe C**, Pilz T, Klostermann C, Berna M, Schild HH, Sauerbruch T, Caselmann WH. Clinical characteristics and outcome of a cohort of 101 patients with hepatocellular carcinoma. *World J Gastroenterol* 2001; **7**: 208-215
9 **Yip D**, Findlay M, Boyer M, Tattersall MH. Hepatocellular carcinoma in central sydney: a 10-year review of patients seen in a medical oncology department. *World J Gastroenterol* 1999; **5**: 483-487
10 **Fan J**, Ten GJ, He SC, Guo JH, Yang DP, Wang GY. Arterial chemoembolization for hepatocellular carcinoma. *World J Gastroenterol* 1998; **4**: 33-37
11 **Li L**, Wu PH, Li JQ, Zhang WZ, Lin HG, Zhang YQ. Segmental transcatheter arterial embolization for primary hepatocellular carcinoma. *World J Gastroenterol* 1998; **4**: 511-512
12 **Chen MS**, Li JQ, Zhang YQ, Lu LX, Zhang WZ, Yuan YF, Guo YP, Lin XJ, Li GH. High-dose iodized oil transcatheter arterial chemoembolization for patients with large hepatocellular carcinoma. *World J Gastroenterol* 2002; **8**: 74-78
13 **Wang JH**, Lin G, Yan ZP, Wang XL, Cheng JM, Li MQ. Stage II surgical resection of hepatocellular carcinoma after TAE: A report of 38 cases. *World J Gastroenterol* 1998; **4**: 133-136
14 **Sithinamsuwan P**, Piratvisuth T, Tanomkiat W, Apakupakul N, Tongyoo S. Review of 336 patients with hepatocellular carcinoma at songklanagarind hospital. *World J Gastroenterol* 2000; **6**: 339-343
15 **Schmid R**. Prospect of gastroenterology and hepatology in the next century. *World J Gastroenterol* 1999; **5**: 185-190
16 **Kinoshita H**, Sakai K, Hirohashi K, Igawa S, Yamasaki O, Kubo S. Preoperative portal vein embolization for hepatocellular carcinoma. *World J Surg* 1986; **10**: 803-808
17 **Elias D**, Ouellet JF, De Baere T, Lasser P, Roche A. Preoperative selective portal vein embolization before hepatectomy for liver metastases: long-term results and impact on survival. *Surgery* 2002; **131**: 294-299
18 **Azoulay D**, Castaing D, Smail A, Adam R, Cailliez V, Laurent A, Lemoine A, Bismuth H. Resection of nonresectable liver metastases from colorectal cancer after percutaneous portal vein embolization. *Ann Surg* 2000; **231**: 480-486
19 **Wakabayashi H**, Okada S, Maeba T, Maeta H. Effect of preoperative portal vein embolization on major hepatectomy for advanced-stage hepatocellular carcinomas in injured livers: a preliminary report. *Surg Today* 1997; **27**: 403-410
20 **Wakabayashi H**, Yachida S, Maeba T, Maeta H. Evaluation of liver function for the application of preoperative portal vein embolization on major hepatic resection. *Hepatogastroenterology* 2002; **49**: 1048-1052
21 **Tominaga M**, Ku Y, Iwasaki T, Fukumoto T, Muramatsu S, Kusunoki N, Suzuki Y, Fujino Y, Kuroda Y. Effect of portal vein embolization on function of the nonembolized lobes of the liver: Evaluation by first-pass hepatic lidocaine extraction in dogs. *Surgery* 2002; **132**: 424-430
22 **Nagino M**, Kamiya J, Kanai M, Uesaka K, Sano T, Yamamoto H, hayakawa N, Nimura Y. Right trisegment portal vein embolization for biliary tract carcinoma: Technique and clinical utility. *Surgery* 2000; **127**: 155-160
23 **Imamura H**, Shimada R, Kubota M, Matsuyama Y, Nakayama A, Miyagawa S, Makuuchi M, Kawasaki S. Preoperative portal vein embolization: an audit of 84 patients. *Hepatology* 1999; **29**: 1099-1105
24 **Gerunda GE**, Bolognesi M, Neri D, Merenda R, Miotto D, Barbazza F, Zangrandi F, Bisello M, Valmasoni M, Gangemi A, Gagliesi A, Faccioli AM. Preoperative selective portal vein embolization (PSPVE) before major hepatic resection. Effectiveness of doppler estimation of hepatic blood flow to predict the hypertrophy rate of non-embolized liver segments. *Hepatogastroenterology* 2002; **49**: 1405-1411
25 **Kubo S**, Shiomi S, Tanaka H, ShutoT, Takemura S, Mikami S, Uenishi T, Nishino Y, Hirohashi K, Kawamura E, Kinoshita H. Evaluation of the effect of portal vein embolization on liver function by (99m)tc-galactosyl human serum albumin scintigraphy. *J Surg Res* 2002; **107**: 113-118
26 **De Baere T**, Roche A, Elias D, Lasser P, Lagrange C, Bousson V. Preoperative portal vein embolization for extension of hepatectomy indications. *Hepatology* 1996; **24**: 1386-1391
27 **Abdalla EK**, Barnett CC, Doherty D, Curley SA, Vauthey JN. Extended hepatectomy in patients with hepatobiliary malignancies with and without preoperative portal vein embolization. *Arch Surg* 2002; **137**: 675-680
28 **Gerunda GE**, Neri D, Merenda R, Barbazza F, Zangrandi F,

Meduri F, Bisello M, Valmasoni M, Gangemi A, Faccioli AM. Effectiveness of preoperative selective portal vein embolization before extensive hepatic resection. *Liver Transpl* 2002; **8**: 405-407

29 **Sugawara Y**, Yamamoto J, Higashi H, Yamasaki S, Shimada K, Kosuge T, Takayama T, Makuuchi M. Preoperative portal embolization in patients with hepatocellular carcinoma. *World J Surg* 2002; **26**: 105-110

30 **Lee KC**, Kinoshita H, Hirohashi K, Kubo S, Iwasa R. Extension of surgical indications for hepatocellular carcinoma by portal vein embolization. *World J Surg* 1993; **17**: 109-115

31 **Wakabayashi H**, Ishimura K, Okano K, Karasawa Y, Goda F, Maeba T, Maeta H. Application of preoperative portal vein embolization before major hepatic resection in patients with normal or abnormal liver parenchyma. *Surgery* 2002; **131**: 26-33

32 **Tanaka H**, Hirohashi K, Kubo S, Shuto T, Higaki I, Kinoshita K. Preoperative portal vein embolization improves prognosis after right hepatectomy for hepatocellular carcinoma in patients with impaired hepatic function. *Br J Surg* 2000; **87**: 879-882

33 **Harada H**, Imamura H, Miyagawa S, Kawasaki S. Fate of the human liver after hemihepatic portal vein embolization: Cell kinetic and morphometric study. *Hepatology* 1997; **26**: 1162-1170

34 **Shimizu Y**, Suzuki H, Nimura Y, Onoue S, Nagino M, Tanaka M, Ozawa T. Elevated mitochondrial gene expression during rat liver regeneration after portal vein ligation. *Hepatology* 1995; **22**: 1222-1229

35 **Chijiiwa K**, Saiki S, Noshiro N, Kameoka N, Nakano K, Tanaka M. Effect of preoperative portal vein embolization on liver volume and hepatic energy status of the nonembolized liver lobe in humans. *Eur Surg Res* 2000; **32**: 94-99

36 **Kawai M**, Naruse K, Komatsu S, Kobayashi S, Nagino M, Nimura Y, Sokabe M. Mechanical stress-dependent secretion of interleukin 6 by endothelial cells after portal vein embolization: Clinical and experimental studies. *J Hepatol* 2002; **37**: 240-246

37 **Uemura T**, Miyazaki M, Hirai R, Matsumoto H, Ota T, Ohashi R, Shimizu N, Tsuji T, Inoue Y, Namba M. Different expression of positive and negative regulators of hepatocyte growth in growing and shrinking hepatic lobes after portal vein branch ligation in rats. *In J Mol Med* 2000; **5**: 173-179

38 **Tsuge H**, Mimura H, Kawata N, Orita K. Right portal vein embolization before extended right hepatectomy using laparoscopic catheterization of the ileocolic vein: a prospective study. *Surg Laparosc Endosc* 1994; **4**: 258-263

39 **Lu MD**, Chen JW, Xie XY, Liang LJ, Huang JF. Portal vein embolization by fine needle ethanol injection: experimental and clinical studies. *World J Gastroenterol* 1999; **5**: 506-510

40 **Seymour K**, Manas D, Charnley RM. During liver regeneration following right portal vein embolization the growth rate of liver metastases is more rapid than that of the liver parenchyma. *Br J Surg* 1999; **86**: 1482-1483

41 **Madoff DC**, Hicks ME, Vauthey JN, Charnsangavej C, Morello FA Jr, Ahrar K, Wallace MJ, Gupta S. Transhepatic portal vein embolization: anatomy, indications, and technical considerations. *Radiographics* 2002; **22**: 1063-1076

42 **Tanaka H**, Hirohashi K, Kubo S, Ikebe T, Tsukamoto T, Hamba H, Shuto T, Wakasa K, Kinoshita H. Influence of histological inflammatory activity on regenerative capacity of liver after percutaneous transhepatic portal vein embolization. *J Gastroenterol* 1999; **34**: 100-104

43 **Kaneko T**, Nakao A, Takagi H. Clinical studies of new material for portal vein embolization: Comparison of embolic effect with different agents. *Hepatogastroenterology* 2002; **49**: 472-477

44 **Yamakado K**, Takeda K, Nishide Y, Jin J, Matsumura K, Nakatsuka A, Hirano T, Kato N, Nakagawa T. Portal vein embolization with steel coil and absolute ethanol: a comparative experimental study with canine liver. *Hepatology* 1995; **22**: 1812-1818

45 **Lu MD**, YY Y, Ren W. A study of portal vein embolization with absolute ethanol injection in cirrhotic rats. *World J Gastroenterol* 1998; **4**: 415-417

46 **Lu MD**, Liang LJ, Huang JF, Ye WJ, Yang QS, Peng BG, Xie XY. Portal vein embolization with ethanol injection via a fine needle in dogs. *Surg Today* 1995; **25**: 416-420

Edited by Zhang JZ and Wang XL