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Portal Vein Embolization Before Right Hepatectomy

Prospective Clinical Trial

Olivier Farges, MD, PhD,* Jacques Belghiti, MD,* Reza Kianmanesh, MD,* Jean Marc Regimbeau, MD,* Roberto Santoro, MD,* Valérie Vilgrain, MD,† Alban Denys, MD,† and Alain Sauvanet, MD*

*From the Hepatobiliary Service and Department of *Digestive Surgery and †Radiology, Beaujon Hospital, Assistance Publique, Clichy, France*

Objective
To assess the impact of liver hypertrophy of the future liver remnant volume (FLR) induced by preoperative portal vein embolization (PVE) on the immediate postoperative complications after a standardized major liver resection.

Summary Background Data
PVE is usually indicated when FLR is estimated to be too small for major liver resection. However, few data exist regarding the exact quantification of sufficient minimal functional hepatic volume required to avoid postoperative complications in both patients with or without chronic liver disease.

Methods
All consecutive patients in whom an elective right hepatectomy was feasible and who fulfilled the inclusion and exclusion criteria between 1998 and 2000 were assigned to have alternatively either immediate surgery or surgery after PVE. Among 55 patients (25 liver metastases, 2 cholangiocarcinoma, and 28 hepatocellular carcinoma), 28 underwent right hepatectomy after PVE and 27 underwent immediate surgery. Twenty-eight patients had chronic liver disease. FLR and estimated rate of functional future liver remnant (%FFLR) volumes were assessed by computed tomography.

Results
The mean increase of FLR and %FFLR 4 to 8 weeks after PVE were respectively 44 ± 19% and 16 ± 7% for patients with normal liver and 35 ± 28% and 9 ± 3% for those with chronic liver disease. All patients with normal liver and 86% with chronic liver disease experienced hypertrophy after PVE. The postoperative course of patients with normal liver who underwent PVE before right hepatectomy was similar to those with immediate surgery. In contrast, PVE in patients with chronic liver disease significantly decreased the incidence of postoperative complications as well as the intensive care unit stay and total hospital stay after right hepatectomy.

Conclusions
Before elective right hepatectomy, the hypertrophy of FLR induced by PVE had no beneficial effect on the postoperative course in patients with normal liver. In contrast, in patients with chronic liver disease, the hypertrophy of the FLR induced by PVE decreased significantly the rate of postoperative complications.

Despite the decrease in postoperative complications after liver resection over the past 10 years,[1–12] there is theoretical evidence that an insufficient hepatic functional reserve estimated by a small future liver remnant volume (FLR) after major liver resection is still considered a risky situation.[2,3,11,13–18] Therefore, it could be assumed that by hypertrophying the FLR, the safety and tolerance of major liver resections could be improved.[13,18–37]

Based on this argument, portal vein embolization (PVE) has been increasingly used during recent years with minimal side effects, especially for major liver resection requiring the removal of a large quantity of functional liver parenchyma.[13,18–37] PVE has been used in both patients with or without chronic liver disease who have diseases such as cholangiocarcinoma,[31,32,35] hepatocellular carcinoma (HCC),[20,37] and liver metastases.[21–25,28]

Correspondence: Jacques Belghiti, MD, Department of Digestive Surgery, Hospital Beaujon, 100, Boulevard du Général Leclerc, 92118 Clichy Cedex, France.
E-mail: j.bel@bjn.ap-hop-paris.fr
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However, because few data exist regarding the exact quantification of the minimal functional hepatic volume required to avoid postoperative complications, the indications for PVE remain arbitrary.[13] Usually PVE is performed so that resection can be performed in patients with apparently unresectable disease, especially when the FLR accounts for less than 25% to 35% of the whole liver in patients with normal liver parenchyma[13,17,18,21,24] and less than 40% in patients with chronic liver disease.[13,20] Some groups have extended their indications for hepatectomy corresponding to the removal of more than 55% of the whole liver volume whatever the status of the nontumorous liver parenchyma.[25] Regarding results of retrospective trials, PVE effects are either reported descriptively alone or in comparison with historical or parallel-matched controls who did not fulfill the previously noted criteria for PVE.[20,21,24,25,27,31,33,36–38]

We designed a prospective comparative trial to measure the impact of preoperative PVE on the postoperative course of a group of patients who underwent the same standardized major hepatectomy. The results were then stratified by the presence of normal liver parenchyma or an underlying chronic liver disease with fibrosis.

METHODS

Patients

Between November 1998 and December 2000, all consecutive patients in whom a right hepatectomy (removal of Couinaud segments 5, 6, 7, and 8) was planned in the Department of Liver Surgery, Beaujon Hospital, were considered as potential candidates for this trial when they fulfilled the following inclusion criteria: technically feasible right hepatectomy for liver metastases or primary liver tumors with no other tumors in the left liver or previous history of liver resection; in patients with HCC, nontumorous liver biopsy assessing the presence or absence of chronic liver disease; in patients with chronic liver disease, absence of impaired preoperative liver function (Child-Pugh score A), including conjugate bilirubin less than 35 μmol/L and prothrombin time more than 75% of normal controls; fully patent right portal vein and bile duct; availability of pre-embolization and preoperative computed tomography scan volumetry; exclusive abdominal incision without opening of the pleural cavity; absence of simultaneous extrahepatic liver surgery. Exclusion criteria were as follows: age more than 75 or less than 16 years; ASA score risk 3 or more;[39] less than 2 months' delay between preoperative systemic chemotherapy or transarterial chemoembolization and surgery; extrahepatic metastases (peritoneum, pulmonary, bone marrow, brain); preoperative biliary drainage or portal vein obstruction; preoperative signs of systemic or biliary infection (cholangitis); ascites detected on ultrasonography; in patients with chronic liver disease, more than twice the normal upper range values for ALT; receiving interferon therapy; tumor invasion of the retrohepatic vena cava and/or of the trunk of the right hepatic vein; serum creatinine more than 120 μmol/L.

Study Design

The protocol was approved by the local ethics committee. Patients were informed about possible benefits and complications of both PVE and liver surgery before their inclusion in the study. Patients were not randomized but were prospectively assigned to have alternatively either immediate surgery or surgery after PVE. There were 59 initial inclusions, and 31 had PVE. Indications for liver resection were liver metastases in 28 (including 25 from colorectal cancer), intrahepatic cholangiocarcinoma in 2, and HCC in 29. Three patients with colorectal liver metastases could not undergo right hepatectomy and were excluded from the study: two for presence of peritoneal carcinomatosis at laparotomy (one after PVE) and one for progression of liver metastases before surgery (after PVE). One patient with HCC developed ascites after PVE and did not undergo resection. Finally, among the 55 patients who fulfilled all of the inclusion and exclusion criteria, 27 were allocated to have immediate surgery and 28 surgery after PVE.

Status of Liver Parenchyma

Status of the nontumorous liver parenchyma was defined according to the classification of Knodell et al:[40] grade 0, no sign of fibrosis; grade 1, fibrous portal expansion; grade 3, bridging fibrosis; grade 4, cirrhosis. Patients with a score of 3 or 4 were considered to have a chronic liver disease; patients with a score of 0 or 1 were considered to have normal liver parenchyma. According to this classification, 27 patients had normal liver and 28 had chronic liver disease.

Volumetric Assessment

All patients underwent volumetric helical computed tomography estimation of their liver volumes before PVE and surgery. The mean interval between preoperative volumetry and surgery was 8 ± 6 days. Measurements were performed for the whole liver as well as for the right and left livers, using as landmarks the middle hepatic vein, identified by intravenous bolus injection of contrast, and the gallbladder. The future liver remnant volume (FLR) was considered to be the volume of the left liver (segments 1–4). The estimated rate of future functional liver remnant volume (%FFLR) was calculated after assuming that the density of the liver was close to 1 by using the following formula: %FFLR = (left liver volume $\times$ 100)/(total liver volume - tumor volume). The increase in the left liver volume corresponding to FLR after PVE was calculated using the following formula: (volume of left liver before surgery - volume of left liver before embolization) $\times$ 100/volume of

left liver before embolization). The increase in the %FFLR after PVE was calculated as follows: (%FFLR after PVE) - (%FFLR before PVE).

Right PVE

Right PVE was performed using the contralateral transhepatic approach.[19] In brief, a collateral vein of the left branch of the portal vein was punctured under light general anesthesia and ultrasound guidance. Following control venous portography, the right anterior and posterior portal branches were embolized with a mixture of cyanoacrylate (Histoacryle Braun, Lab, Hamburg, Germany) and lipiodol (Lipiodol ultrafluide, Guerbert Lab, Paris, France). Surgery was performed 4 to 8 weeks after embolization (mean 49 ± 13 days).

Technique of Right Hepatectomy

All patients underwent liver resection by one of the three senior liver surgeons of our department (JB, OF, AS) using a standardized technique for right hepatectomy. In brief, the abdomen was opened through a bisubcostal or a J-shaped incision without phrenotomy. The portal pedicle was encircled with a tape. The falciform and right triangular ligaments were sectioned and the right liver up to the retrohepatic vena cava was totally mobilized by section and sutures of the accessory right hepatic veins and the hepatocaval ligament. The right hepatic vein was controlled in an extrahepatic plane and encircled with a tape. Parenchymal transection was performed by either clamp-crush technique or with an ultrasound aspiration dissector (Dissectron, Satelec Médical, Mérignac-France) under intermittent clamping of the hepatic pedicle as previously described.[41] At the end of the procedure, methylene blue was injected into the biliary ducts through a drain previously placed in the cystic duct that was thereafter removed. A multiperforated 27-F drain was left in the right hypochondrium at the end of the procedure, and the abdomen was closed with continuous sutures. Patients were routinely transferred to the intensive care unit and were returned to the wards at the discretion of the intensivist.

Endpoints

The main assessed endpoints were the global in-hospital mortality and morbidity rates; the units of blood transfused; the incidence, nature, and number of patients with one or several postoperative complications; the kinetics of post-PVE and postoperative serum bilirubin, AST, ALT, alkaline phosphatase, and gamma glutamyl transpeptidase (γGT) levels; and the duration of intensive care unit and overall hospital stays.

Postoperative pulmonary complications included all clinically symptomatic pleural effusions, atelectasis, or infections. Postoperative ascites was defined by an abdominal drain output greater than 500 mL/d; asymptomatic ascites discovered by ultrasound was not included. Renal failure was defined as a serum creatinine level greater than 150 μmol/L. Liver failure was defined by a prothrombin time of less than 50% (of normal) and/or by serum bilirubin more than 50 μmol/L on postoperative day 5 or thereafter.

Statistical Analysis

Comparison of liver function test results before and after PVE was performed using the sign test. The Fisher exact test and the Mann-Whitney test were used for quantitative variables. Comparison between qualitative variables was performed using the chi-square test. Data are expressed as mean ± SD. At $P > 0.05$, the difference was considered not significant.

RESULTS

Population Characteristics

Patients in the two groups (with and without preoperative PVE) were similar in terms of clinical, biologic, and volumetric variables as well as indication and the number of patients with underlying chronic liver disease (Table 1). In the subgroup of patients with normal liver, the two groups (with and without preoperative PVE) had similar clinical, biologic, and volumetric characteristics (Table 2). In the subgroup of patients with chronic liver disease, all underwent surgery for HCC; the two groups (with and without preoperative PVE) had similar clinical, biologic, and volumetric characteristics and the rate of patients with cirrhosis was identical in the two groups (Table 3).

Liver Function Tests After PVE

PVE was successfully completed without complication in all of the patients. All patients were discharged 2 to 5 days after the PVE. As shown in Figure 1, liver function tests after PVE and before surgery showed no changes in prothrombin time, a slight increase in total serum bilirubin after PVE (especially in patients with chronic liver disease), and a significant peak in transaminase after PVE (especially in patients with normal liver). All of the results returned to pre-PVE values except for γGT and alkaline phosphatases, which increased continuously.

Volumetry After PVE

In patients with normal liver, the volume of the left liver (FLR) increased from 442 ± 138 mL (range 276–723) to 626 ± 172 mL (range 400–924) ($P < .01$). The mean

Table 1. PATIENT CHARACTERISTICS

	PVE (n = 27)	No PVE (n = 28)	*P* Value
Male (n pts)	18 (67%)	16 (57%)	NS
Age (years)	58 ± 13	53 ± 17	NS
Body weight (kg)	72 ± 14	69 ± 13	NS
Metastases (n pts)	12 (44%)	13 (46%)	NS
Colorectal	10	12	NS
Endocrine	2	1	NS
Primary tumors (n pts)	15 (56%)	15 (54%)	NS
Hepatocellular carcinoma	14	14	NS
Intrahepatic cholangiocarcinoma	1	1	NS
Mean tumor diameter (cm)	6.5 ± 3	7.5 ± 4	NS
Nontumorous liver status			
Normal	13 (48%)	14 (50%)	NS
Chronic liver disease*	14 (52%)	14 (50%)	
Total liver volume (mL)	1,651 ± 441	1,683 ± 648	NS
Total liver volume − tumor volume (mL)	1,430 ± 380	1,444 ± 523	NS
FLR (mL)	473 ± 202	491 ± 192	NS
%FFLR	33 ± 10	34 ± 15	NS

* Corresponding to score 3 or 4 fibrosis at the biopsy of the nontumorous liver parenchyma.
FLR, future remnant liver volume corresponding to the left liver volume (Couinaud segments 1 to 4); %FFLR: estimated rate of functional remnant liver volume = (left liver volume × 100)/(Total liver volume − tumor volume).

increase of the left liver volume (FLR) induced by PVE was 44 ± 19% (range 20–76%). After PVE the %FFLR increased from 31 ± 6% to 47 ± 11%, representing a median increase of 16 ± 7% (range 8–28%).

In patients with chronic liver disease, the volume of the left liver (FLR) increased from 488 ± 235 mL (range 204–995 mL) to 605 ± 179 mL (range 337–982 mL) ($P < .05$). The mean increase of the left liver volume (FLR) induced by PVE was 35 ± 28% (range −18–68%). After PVE, the %FFLR increased from 35 ± 13% to 44 ± 13%, representing a median increase of 9 ± 3% (range 4–15%).

All patients with normal livers experienced hypertrophy, while 12 of 14 (86%) patients with chronic liver disease had hypertrophy. The two patients whose left liver volume did not increase after PVE had cirrhosis; one of them had a spontaneous portosystemic shunt.

Table 2. CHARACTERISTICS OF PATIENTS WITH NORMAL LIVER PARENCHYMA

	PVE (n = 13)	No PVE (n = 14)	*P* Value
Male (n pts)	6 (46%)	7 (50%)	NS
Age (years)	55 ± 15	52 ± 17	NS
Diabetes mellitus (n pts)	2 (15%)	1 (7%)	NS
Body weight (kg)	70 ± 18	68 ± 14	NS
Metastases (n pts)			
Colorectal	10 (77%)	12 (86%)	NS
Endocrine	2 (15%)	1 (7%)	NS
Primary tumor (n pts)			
Intrahepatic cholangiocarcinoma	1 (8%)	1 (7%)	NS
Tumor diameter (cm)	6 ± 3	8 ± 5	NS
Total bilirubin (μmol/L)	13 ± 6	11 ± 4	NS
Prothrombin time (% of normal)	93 ± 12	95 ± 16	NS
AST (IU/L)	21 ± 11	33 ± 22	NS
Alk. phosph. (IU/L)	101 ± 47	165 ± 106	NS
γGT (IU/L)	46 ± 27	79 ± 70	NS
Total liver volume (mL)	1,634 ± 375	1,718 ± 780	NS
Total liver volume − tumor volume (mL)	1,451 ± 373	1,456 ± 510	NS
FLR (mL)	442 ± 138	483 ± 213	NS
%FFLR (range)	31 ± 7 (20–51)	30 ± 7 (20–60)	NS

FLR, future remnant liver volume corresponding to the left liver volume (Couinaud segments 1 to 4); %FFLR: estimated rate of functional remnant liver volume = (left liver volume × 100)/(total liver volume − tumor volume).

Table 3. CHARACTERISTICS OF PATIENTS WITH CHRONIC LIVER DISEASE

	PVE (n = 14)	No PVE (n = 14)	*P* Value
Male (n pts)	12 (86%)	9 (64%)	NS
Age (years)	60 ± 11	53 ± 17	NS
Diabetes mellitus (n pts)	4 (29%)	3 (21%)	NS
Body weight (kg)	74 ± 9	69 ± 12	NS
Etiology of chronic liver disease	9 (64%)	11 (76%)	NS
Hepatitis B virus	4	7	
Hepatitis C virus	5	4	
Hepatocellular carcinoma (n pts)	14 (100%)	14 (100%)	NS
Tumor diameter (cm)	7 ± 2	7 ± 4	NS
Cirrhosis* (n pts)	7 (50%)	7 (50%)	NS
Total bilirubin (μmol/L)	15 ± 7	16 ± 5	NS
Prothrombin time (% of normal)	87 ± 12	88 ± 11	NS
AST (IU/L)	57 ± 31	63 ± 35	NS
Alk. phosph. (IU/L)	120 ± 56	160 ± 111	NS
γGT (IU/L)	170 ± 170	216 ± 188	NS
Liver volume (mL)	1,668 ± 487	1,649 ± 516	NS
Liver volume − tumor volume (mL)	1,401 ± 368	1,432 ± 537	NS
FLR (mL)	488 ± 235	584 ± 178	NS
%FFLR (range)	35 ± 13 (20–58)	39 ± 24 (24–62)	NS

* Corresponding to score 4 fibrosis at the biopsy of the nontumorous liver parenchyma.
FLR, future remnant liver volume corresponding to the left liver volume (Couinaud segments 1 to 4); %FFLR: estimated rate of functional remnant liver volume = (left liver volume × 100)/(total liver volume − tumor volume).

Excluding these two patients, the mean percentage of the left liver volume (FLR) increase after PVE was 44 ± 19% (range 11–68%).

Intraoperative and Postoperative Course After Right Hepatectomy in Patients With Normal Liver

The number of patients who underwent surgery after PVE or who underwent immediate surgery who required blood transfusion was comparable (4 vs. 3 patients) as well as the amount of transfused units (mean of 2.5 vs. 3 units per patient). Three patients in each group developed postoperative complications, for a morbidity rate of 22% (6/27). All six patients had significant right pleural effusions and/or atelectasis that did not require invasive treatment. Two of these patients experienced additional complications. One in the PVE group required reoperation 12 hours after surgery for persistent bleeding from the abdominal drainage; the other, who had no PVE, experienced a transient biliary leak that did not require specific treatment and healed spontaneously. The kinetics of postoperative liver function tests are summarized in Figure 2. Serum bilirubin, transaminase, and prothrombin time were almost identical in the two groups, as well as the kinetics of alkaline phosphatase and γGT. Mean hospital stay was the same in patients with normal liver parenchyma with or without PVE: respectively, 12 ± 4 versus 13 ± 4 days (P = NS).

Outcome After Right Hepatectomy in Patients With Chronic Liver Disease

The number of patients with or without PVE who required blood transfusion was comparable (5 vs. 4 patients), as well as the amount of transfused units (2.5 vs. 3 units per patient). As shown in Table 4, the number of patients who had one or more complications was significantly lower when right hepatectomy was performed after PVE (7 vs. 13, $P < .05$). The incidence of pulmonary complications, ascites, and liver failure was also significantly lower when right hepatectomy was performed after PVE. The incidence of sepsis was lower in patients having preoperative PVE, although the difference was not significant. One patient in each group, both with cirrhosis, died of these complications (liver failure and sepsis) on postoperative days 20 and 46. In the PVE group, the %FFLR of the patient who died and also failed to hypertrophy after PVE was 48%. The %FFLR of the patient who died in the group without PVE was 46%.

The kinetics of postoperative liver function tests are summarized in Figure 3. The postoperative serum bilirubin level was significantly higher and the prothrombin time significantly lower in the nonembolized group at all postoperative time points ($P < .05$). AST level was also significantly higher in the nonembolized group on postoperative days 1, 3, and 5 ($P < .05$). A significantly shorter intensive care unit stay (6 ± 3 vs. 15 ± 10 days, $P < .05$) and in-hospital stay (13 ± 4 vs. 30 ± 15 days, $P < .001$) were observed after PVE.

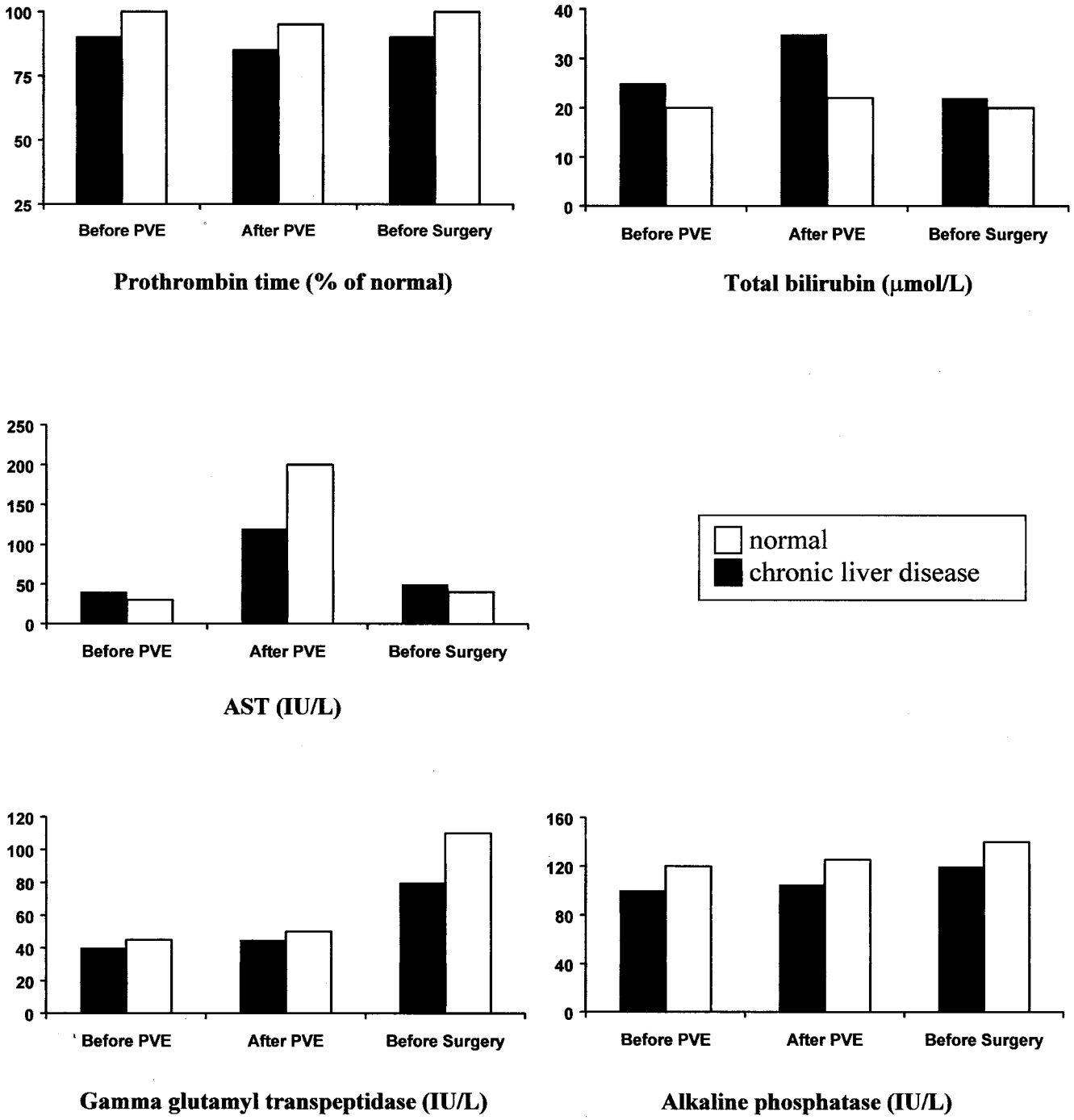

Figure 1. Liver function tests before portal vein embolization (PVE), after PVE, and before surgery in patients with normal liver and chronic liver disease. For transaminase, the peak value of aspartate aminotransferase was assessed before PVE, within 5 days after PVE, and within 5 days before surgery. At the time of surgery, all test results returned to pre-PVE values, except for gamma glutamyl transpeptidase and alkaline phosphatase, which increased continuously.

DISCUSSION

This study focused on the benefits of hypertrophy of the FLR induced by preoperative PVE in terms of postoperative complications in patients undergoing a standardized major liver resection and showed that the safety and tolerance of right hepatectomy were significantly increased in patients with chronic liver disease, while no benefit was found in patients with normal liver parenchyma.

Multiple studies have shown that PVE is effective in inducing hypertrophy of the nonembolized liver segments,

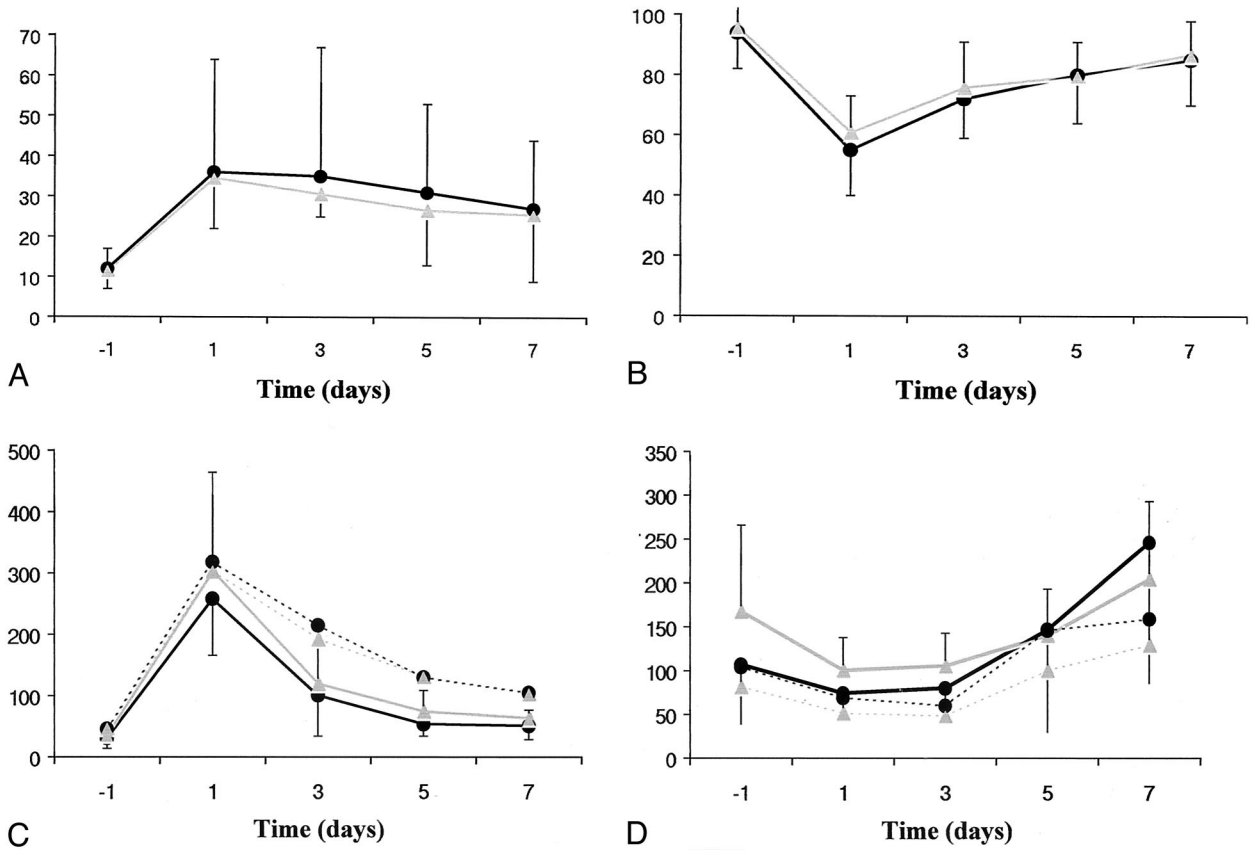

Figure 2. Postoperative kinetics of liver function tests in patients with no or minimal fibrosis of the nontumorous liver undergoing right hepatectomy with (circles) or without (triangles) preoperative portal vein embolization. Values are expressed as mean ± SD. (A) Serum bilirubin (μmol/L). (B) Prothrombin time expressed as a percentage of normal controls. (C) AST (plain line) and ALT (broken line) (IU/L). (D) Alkaline phosphatase (plain line) (IU/L) and gamma glutamyl transpeptidase (broken line) (IU/L).

allowing us to perform major resection in patients with a low %FFLR.[13] However, the potential benefits of this procedure have not been validated by prospective studies. Existing series have studied patients with various underlying liver diseases, including steatotic, cholestatic, fibrotic, and cirrhotic parenchyma. Additionally, these studies included heterogeneous techniques of PVE (ileal, transhepatic, balloon), various materials for embolization (gels, glue, acrylates, lipidic solutions, ethanol, coils), various extents of surgical procedures, and various assessment of FLR.[13,18,42] Vauthey et al[18] proposed the use of formulas based on the body surface area, avoiding the subtraction of the tumor volume and taking into account atrophic hypertrophic changes in cirrhotic livers. Thus, difficulties persist in determining the minimal hepatic volume required to avoid postoperative complications. Therefore, the indications for PVE are somewhat arbitrary for variable ratios of %FFLR ranging from 25% to more than 40%.[13,18]

We designed this comparative prospective trial with important selective conditions to measure the impact of preoperative PVE on the postoperative course of patients undergoing a standardized type of liver resection. Right hepatectomy was planned in selected candidates because this type of resection has already been used as a reference type of standardized major liver resection.[5,6,8,43] To homogenize the treated population, we excluded patients requiring associated gastrointestinal surgical procedures such as colorectal surgery. The right hepatectomy was planned in patients with a mean %FFLR of 33%, a rate that fulfilled the criteria usually used for preoperative PVE in previous studies.[13] In the present study, the aim of PVE was not to convert unresectable patients to resectable, as has been suggested by others,[13,20,21,24,28] but rather to compare its potential effects in terms of postoperative complications related to a standardized major liver surgery. Furthermore, we excluded patients having so-called injured liver: those with severe steatosis, cholestasis, or systemic or arterial chemotherapies.[20,24,33] The severity of the inclusion and exclusion criteria led us to focus on patients with normal liver parenchyma and those with either fibrotic or cirrhotic liver parenchyma.

The mean increases of %FFLR 4 to 8 weeks after PVE in both patients with normal liver and with chronic liver disease, respectively 16% and 9%, were in accordance with other series that reported 2 to 9 weeks after PVE a mean increase in %FFLR of 12 ± 5%.[13] The kinetics of post-PVE

Table 4. POSTOPERATIVE COURSE AFTER RIGHT HEPATECTOMY WITH OR WITHOUT PREOPERATIVE PVE IN PATIENTS WITH CHRONIC LIVER DISEASE

	PVE (n = 14)	No PVE (n = 14)	*P* Value
In-hospital mortality (n pts)	1§	1	.76
Age (years)	67	56	
Cirrhosis (grade 4)	1	1	
Liver failure*	1	1	
Uncontrolled sepsis	1	1	
%FFLR before surgery	48	46	
Uneventful course (n pts)	7	1	.012
Patients with one or more complications	7	13	.012
Details of complications			
Pulmonary	4§	13	.0007
Sepsis	1§	5	.08
Hemorrhage	1	3	.29
Liver failure*	1§	7	.01
Renal failure†	2§	1	.50
Ascites	4	10	.03
Stay in ICU‡ (days)	5 ± 3	12 ± 10	.002
In-hospital stay‡ (days)	13 ± 4	30 ± 15	.0002

%FFLR, estimated rate of functional remnant liver volume = (left liver volume × 100)/(volume of whole liver − tumor volume).
* Defined by a prothrombin time <50% and/or serum bilirubin >50 μmol/L on postoperative day 5 or thereafter.
† Defined as a serum creatinine level >150 μmol/L.
‡ Excluding two patients who died.
§ Corresponding to or including the two cirrhotic patients who failed to increase the volume of left liver following PVE.

biologic liver tests were similar to those reported in other studies, except the continuous increase for γGT and PAL until surgery. This observation might be related to liver hypertrophy of the nonembolized liver.

In patients with normal liver parenchyma, our results showed that the postoperative course after right hepatectomy in patients with a mean %FFLR of 31% was similar to those with 40%. Therefore, it appears that the significant hypertrophy of the left liver induced by PVE had no measurable impact in terms of postoperative complications. Intraoperative blood loss, the incidence and type of postoperative complications, postoperative kinetics of liver function tests, and the length of hospital stay were remarkably similar in patients undergoing right hepatectomy with or without preoperative PVE. Although Vauthey et al[18] suggested performing PVE in patients with normal liver when the %FFLR is no more than 25%, the inferior limits of functional liver volume in patients with normal parenchyma to avoid postoperative liver failure remains unknown. Unless there are no additional risk factors such as injured liver (i.e., chemotherapy, major steatosis or cholestasis), very extended liver resections, or associated major gastrointestinal surgery,[24,27,28,31–33,35,38] we found no arguments for inducing hypertrophy of the FLR before standard right hepatectomy in a patient with normal liver. We believe that PVE should be seriously discussed on a patient-by-patient basis because of the possible risk of tumor growth induced by PVE in the contralateral liver.[44,45]

In contrast, the impact of PVE in patients with fibrotic or cirrhotic livers was so obvious, especially when it was associated with an increase in the volume of the left liver, that we decided to adopt routine performance of PVE before major hepatectomy in patients with chronic liver disease. Eighty-six percent of patients with chronic liver disease who had fibrotic liver parenchyma grade 3 or grade 4 (cirrhosis) experienced hypertrophy of the nonembolized liver, with a mean increase in volume of 44%. These results are similar to those reported by other studies, in which the reported rate of increase of the nonembolized liver segments after PVE ranged from 30% to 90%.[13,20,37,46] In fibrotic or cirrhotic patients who had experienced hypertrophy of the nonembolized liver parenchyma after PVE, the incidence of postoperative complications and the length of hospital stay were significantly reduced (more than two-fold) and became almost comparable to those observed in patients with normal liver. Similarly, the analysis of the kinetics of liver function tests showed that the postoperative parenchymal injury was significantly lower after PVE with regard to the prothrombin time, serum bilirubin, and transaminase after resection; these levels were comparable to those observed following the same liver resection in patients with normal liver.[43]

In 14% of patients, PVE failed to increase the volume of the fibrotic or cirrhotic nontumorous liver. This was similar to the figures reported by others, which varied from 2% to 20%.[13] We believe that the failure to increase the FLR, despite a technically successful PVE, in fibrotic or cirrhotic patients should be considered as an indicator of the inability of the liver parenchyma to regenerate, therefore contraindicating any major liver resection in these patients. This absence of hypertrophy following a technical successful PVE might be considered before major hepatectomy as a dynamic preoperative liver function test in Child grade A cirrhotic patients. Also, we believe that in patients with chronic liver disease, one of the important factors to reduce postoperative complications is not the importance of left liver hypertrophy measured by volumetry, but the induction of left liver hypertrophy by right PVE. This point could allow us to shorten the actual period between PVE and liver resection to less than 4 weeks.[47]

Several reasons could explain the failure of hypertrophy after technically successful PVE, among them the activity of the underlying chronic liver disease, the presence of diabetes,[48] the possible vascular recanalization of the embolized portal vein branches, and the presence of major portal hypertension with portosystemic shunts.[25,46,49] In the present series, one of the patients with chronic liver disease had portal hypertension with a portosystemic shunt, which could have prevented the increase in the portal perfusion to the left liver. Studies showing a significant correlation be-

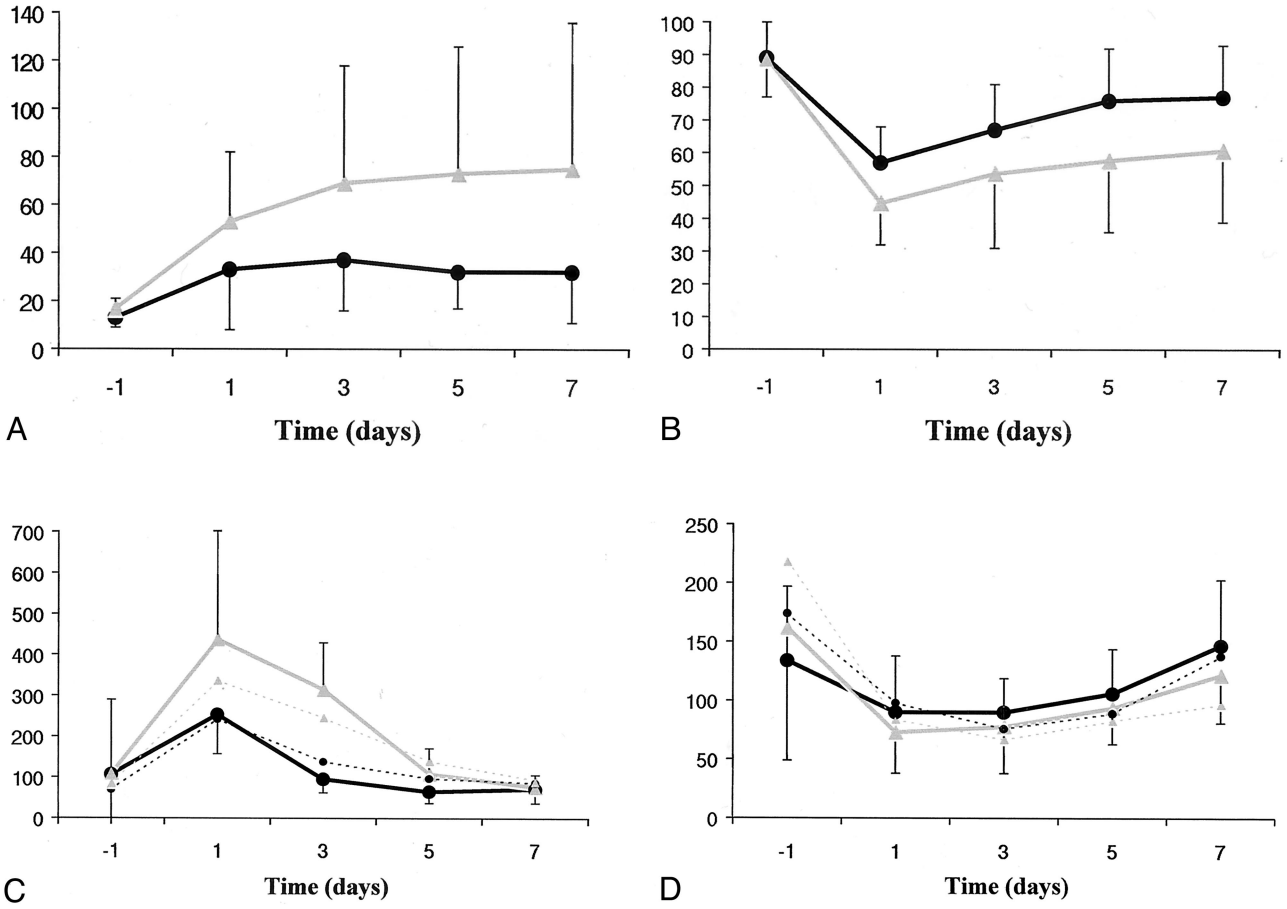

Figure 3. Postoperative kinetics of liver function tests in patients with extensive fibrosis (grade 3) or cirrhosis (grade 4) of the parenchyma of the nontumorous liver undergoing right hepatectomy with (circles) or without (triangles) preoperative portal vein embolization. Values are expressed as mean ± SD. (A) Serum bilirubin (μmol/L). (B) Prothrombin time expressed as a percentage of normal controls. (C) AST (plain line) and ALT (broken line) (UI/L). (D) Alkaline phosphatase (plain line) (UI/L) and gamma glutamyl transpeptidase (broken line) (UI/L).

tween the severity of preoperative portal hypertension and high risk of hepatic failure after liver resection for HCC reinforce the hypothesis for the low capacity of the remaining liver to hypertrophy after surgery in case of high portal pressure.[49,50]

In conclusion, based on the results of the present study, we found no argument for the routine performance of PVE before a right hepatectomy in patients with normal liver. In contrast, we strongly advocate the performance of PVE in patients with chronic liver disease before any major liver resection. In these patients, the absence of hypertrophy of the nonembolized liver following successful PVE should be considered as an indicator of the inability of the liver to regenerate, therefore contraindicating major liver resection.

References

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