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BRIEF ARTICLE

Comparison of percutaneous transhepatic portal vein embolization and unilateral portal vein ligation

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Abstract

AIM: To compare the effect of percutaneous transhepatic portal vein embolization (PTPE) and unilateral portal vein ligation (PVL) on hepatic hemodynamics and right hepatic lobe (RHL) atrophy.

METHODS: Between March 2005 and March 2009, 13 cases were selected for PTPE (n = 9) and PVL (n = 4) in the RHL. The PTPE group included hilar bile duct carcinoma (n = 2), intrahepatic cholangiocarcinoma (n = 2), hepatocellular carcinoma (n = 2) and liver metastasis (n = 3). The PVL group included hepatocellular carcinoma (n = 2) and liver metastasis (n = 2). In addition, observation of postoperative hepatic hemodynamics obtained from computed tomography and Doppler ultrasonography was compared between the two groups.

RESULTS: Mean ages in the two groups were 58.9 ± 2.9 years (PVL group) *vs* 69.7 ± 3.2 years (PTPE group), which was a significant difference (P = 0.0002). Among the indicators of liver function, including serum albumin, serum bilirubin, aspartate aminotransferase, alanine aminotransferase, platelets and indocyanine green retention rate at 15 min, no significant differences were observed between the two groups. Preoperative RHL volumes in the PTPE and PVL groups were estimated to be 804.9 ± 181.1 mL and 813.3 ± 129.7 mL, respectively, with volume rates of 68.9% ± 2.8% and 69.2% ± 4.2%, respectively. There were no significant differences in RHL volumes (P = 0.83) and RHL volume rates (P = 0.94), respectively. At 1 mo after PTPE or PVL, postoperative RHL volumes in the PTPE and PVL groups were estimated to be 638.4 ± 153.6 mL and 749.8 ± 121.9 mL, respectively, with no significant difference (P = 0.14). Postoperative RHL volume rates in the PTPE and PVL groups were estimated to be 54.6% ± 4.2% and 63.7% ± 3.9%, respectively, which was a significant difference (P = 0.0056). At 1 mo after the operation, the liver volume atrophy rate was 14.3% ± 2.3% in the PTPE group and 5.4% ± 1.6% in the PVL group, which was a significant difference (P = 0.0061).

CONCLUSION: PTPE is a more effective procedure than PVL because PTPE is able to occlude completely the portal branch throughout the right peripheral vein.

Key words: Percutaneous transhepatic portal vein embolization; Portal vein ligation; Liver atrophy; Future liver remnant; Two-stage hepatectomy

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INTRODUCTION

Postoperative liver failure may be induced by major hepatectomy, whereby more than 60%-70% of total liver volume is planned for resection in cases such as hilar bile duct carcinoma, hepatocellular carcinoma and liver metastasis. To reduce the risk of postoperative liver failure due to an insufficient volume of functional liver, the well-established percutaneous transhepatic portal vein embolization (PTPE) procedure can be performed prior to major hepatectomy[1-6]. Unilateral portal vein ligation (PVL) is an alternative method that requires laparotomy[7,8]. Although PTPE has since its introduction become the more popular procedure of the two, PVL remains a viable option during the initial stage of a two-stage hepatectomy procedure (TSHP) for cases such as bilobar multiple liver metastases[9-11]. Both of these techniques occlude the unilateral portal vein, with the aim of inducing atrophy of the ipsilateral liver and thus inducing hypertrophy of the future liver remnant (FLR). In the present study, we retrospectively compared the effectiveness of the two techniques by evaluating the postoperative atrophy rate and hemodynamics of the right hepatic lobe (RHL).

MATERIALS AND METHODS

Patient characteristics of the PTPE and PVL groups

Between March 2005 and March 2009, nine patients were selected for PTPE and four for PVL. The mean patient age was 69.7 ± 3.2 years for the PTPE group and 58.9 ± 2.9 years for the PVL group (P = 0.0002). The clinical characteristics of the patients included hilar bile duct carcinoma (n = 2), intrahepatic cholangiocarcinoma (n = 2), hepatocellular carcinoma (n = 2) and liver metastasis (n = 3) in the PTPE group, and the PVL group had hepatocellular carcinoma (n = 2) and liver metastasis (n = 2). The PTPE group included one patient with hepatitis C, one with hepatitis B, and seven positive for hepatitis B virus (HBV) antigen but negative for hepatitis C virus (HCV) antibody. The PVL group included one patient with hepatitis C, one with hepatitis B, and two positive for HBV antigen and negative for HCV antibody.

PTPE cases

Two patients were diagnosed with hilar bile duct carcinoma, based on findings of obstructive jaundice. Endoscopic nasobiliary drainage was first performed. Before conducting an extended right lobectomy, PTPE was performed because the liver volumes to be resected were 70.8% and 70.2% in the two patients.

In the two cases of intrahepatic cholangiocarcinoma, the tumors were 10 cm and 8 cm in diameter, and both were adjacent to the hilar plate. These two patients also underwent a preoperative PTPE because of planned liver resection volumes of 74.2% and 70.5% respectively.

In the two patients with hepatocellular carcinoma, the tumors were 4.0 cm and 3.5 cm in diameter and adjacent to the right Glisson's capsule. In addition, both the tumors recurred after the transarterial embolization procedure. The liver volume to be resected in these cases was 68.3% and 66.1%, respectively. In addition, indocyanine green retention rate at 15 min (ICG R15) was 17% and 18%, respectively, indicating functional liver impairment. Because of these factors, PTPE was performed prior to resection.

In the three patients with liver metastases, multiple lesions in the right lobes were noted after the initial round of chemotherapy. Preoperative PTPE was scheduled because the liver volumes to be resected in the three patients were 65.2%, 66.6% and 68.8%.

PVL cases

Patients with hepatocellular carcinoma in the PVL group presented with lymph node metastasis. The tumors adjacent to the right Glisson's capsule were 5 cm and 4 cm in diameter with ICG R15 of 38.8% and 15.2%, respectively. The planned liver resection volumes were 65.1% and 69.8%, respectively. Thus, PVL was performed on the right portal branch only during the implementation of lymphadenectomy.

Regarding the two liver metastasis cases, the patients had undergone chemotherapy and developed multiple synchronous liver metastases to both lobes, disseminated from ascending colon cancer. Because the liver resection volumes were 66.9% and 74.8%, the right portal vein was ligated. In addition, right colectomy and partial resection of the left hepatic lobe were also performed in both patients.

Indications for resection

Resectability criteria included an FLR of ⩽ 30% of the total liver volume, whereas this criterion was ⩽ 35% for the patients who had liver cirrhosis or underwent neoadjuvant chemotherapy. In addition, the following equation established by Yamanaka *et al*[12,13] and Okamoto *et al*[14] was used to predict posthepatectomy liver failure: Y = -110 + 0.942 × resection rate (%) + 1.36 × ICG retention rate (%) + 1.17 × patient's age + 5.94 × ICG maximal removal rate (mg/kg per minute). With this equation, the patients who had a calculated Y value > 50 points were deemed unresectable.

PVL and PTPE techniques

For all patients, PTPE or PVL was performed on the RHL. PVL was indicated for patients who were to undergo laparotomy for lymphadenectomy or right colectomy. In PTPE, the umbilical portion of the portal vein was punctured, and the right branch of the portal vein was embolized using a mixture of fibrin glue (Beriplast P; CSL Behring, Tokyo, Japan) and iodized oil (Lipiodol; Guerbet, Aulnay-sous-Bois, France). In the PVL cases, preoperative multidetector row computed tomography (CT) was routinely performed to check for the presence of anatomical variants of the right portal vein. The right branch of the portal vein was intraoperatively isolated and ligated. After each method, Doppler ultrasonography was used to confirm that portal blood flow had

Table 1 Clinical characteristics of the study population (mean ± SD)

Variables	PTPE group (n = 9)	PVL group (n = 4)	P value
Age (yr)	69.7 ± 3.2	58.9 ± 2.9	0.0002
Sex (male:female)	7:2	3:1	
Background (HCV:HBV:NBNC)	1:1:7	1:1:2	
Albumin (g/dL)	3.9 ± 0.4	4.0 ± 0.4	0.61
Bilirubin (mg/dL)	0.9 ± 0.4	1.2 ± 0.7	0.35
AST (IU/L)	30.6 ± 12.2	32.3 ± 8.5	0.47
ALT (IU/L)	35.9 ± 29.1	29.3 ± 15.6	0.92
WBC (/mm^3)	6744 ± 3109	5228 ± 1973	0.41
PLT (× 10^4/mL)	22.1 ± 11.0	19.3 ± 9.9	0.76
PT (%)	84.1 ± 10.5	84.5 ± 12.2	0.86
ICG 15 (%)	10.7 ± 7.4	17.5 ± 13.2	0.43
Child pugh (A:B:C)	7:2:0	3:1:0	

PTPE: Percutaneous transhepatic portal vein embolization; PVL: Portal vein ligation; HCV: Hepatitis C virus; HBV: Hepatitis B virus; NBNC: Hepatitis B surface antigen and HCV antibody negative; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; WBC: White blood cells; PLT: Platelet count; PT: Prothrombin time; ICG 15: Indocyanine green retention rate at 15 min.

been occluded in the ligated lobe and that it had been sustained in the FLR.

Follow-up

No patients had any postoperative complications. Although a slight postoperative decline in liver function was noted in some patients, all improved with conservative treatments.

Statistical analysis

Each patient underwent CT volumetry 1 mo before and after each procedure to evaluate volume changes in the RHL, and the values were compared between the two groups. The RHL atrophy rate was estimated by subtracting the RHL volume rate at 1 mo after PTPE or PVL from the preoperative RHL volume rate. The values in each group were compared using the Mann-Whitney test. All analyses were performed using statistical software (JMP 8.0.2 Macintosh; SAS Institute, Japan). Differences were considered statistically significant at $P < 0.05$.

RESULTS

Clinical characteristics of the study population

The mean age of patients was significantly higher in the PTPE group (58.9 ± 2.9 years *vs* 69.7 ± 3.2 years in the PTPE group), which was a significant difference (P = 0.0002). Among the indicators of liver function, including serum albumin, serum bilirubin, asparate aminotransferase, alanine aminotransferase, platelets and ICG R15, no significant differences were observed between the two groups (Table 1).

Volume change of RHL

Preoperative RHL volumes in the PTPE and PVL groups were estimated to be 804.9 ± 181.1 mL and 813.3 ± 129.7 mL, respectively, with volume rates of 68.9% ± 2.8% and 69.2% ± 4.2%, respectively. There were no significant statistical differences in RHL volumes (P = 0.83) and RHL volume rates (P = 0.94).

Table 2 Right hepatic lobe atrophy rate 1 mo after percutaneous transhepatic portal vein embolization or portal vein ligation (mean ± SD)

Variables	PTPE group (n = 9)	PVL group (n = 4)	P value
Preoperative RHL volume (mL)	804.9 ± 181.1	813.3 ± 129.7	0.83
Preoperative RHL volume rate (%)	68.9 ± 2.8	69.2 ± 4.2	0.94
Postoperative RHL volume (mL)	638.4 ± 153.6	749.8 ± 121.9	0.14
Postoperative RHL volume rate (%)	54.6 ± 4.2	63.7 ± 3.9	0.0056
RHL atrophy rate 1 mo postoperation (%)	14.3 ± 2.3	5.4 ± 1.6	0.0061

PTPE: Percutaneous transhepatic portal vein embolization; PVL: Portal vein ligation; RHL: Right hepatic lobe.

At 1 mo after PTPE or PVL, postoperative RHL volumes in the PTPE and PVL groups were estimated to be 638.4 ± 153.6 mL and 749.8 ± 121.9 mL, respectively, which was not a significant difference (P = 0.14). Postoperative RHL volume rates in the PTPE and PVL groups were estimated to be 54.6% ± 4.2% and 63.7% ± 3.9%, respectively, which was a significant difference (P = 0.0056). At 1 mo postoperatively, the liver volume atrophy rate was 14.3% ± 2.3% in the PTPE group and 5.4% ± 1.6% in the PVL group, which was a significant difference (P = 0.0061) (Table 2).

With respect to the findings from imaging, postoperative CT and Doppler ultrasonography data confirmed residual peripheral portal inflow in the right branch of the ligated portal vein in two cases in the PVL group. In contrast, portal venous flow was confirmed as completely occluded in the PTPE group.

Liver resection and postoperative course

PTPE successfully facilitated liver resection for all nine patients, whereas among the four patients who underwent PVL, two with hepatocellular carcinoma remained unresectable after the procedure. An extended right lobectomy was performed for two hilar bile duct carcinomas and two intrahepatic cholangiocellular carcinomas. A right lobectomy was performed in all the other resectable cases. The 11 patients showed no postoperative complications.

DISCUSSION

Through experimentation on rabbits in 1920, Rous *et al*[15] proved that PVL could induce atrophy of the ipsilateral hepatic lobe and hypertrophy of the FLR lobe. Since then, this technique has been clinically applied by Honjo *et al*[16] and has recently been adopted for TSHP for bilobar multiple liver metastases. In the first stage, partial resec-

Figure 1 Computed tomography showing a case of hilar bile duct carcinoma where the right hepatic lobe volume rate decreased from 68.3% to 50.0% at 1 mo after percutaneous transhepatic portal vein embolization. A: Before percutaneous transhepatic portal vein embolization (PTPE) [right hepatic lobe (RHL) volume rate: 68.3%]; B: After PTPE (RHL volume rate: 50.0%); C: The portal vein in the RHL was completely occluded after PTPE.

Figure 2 Computed tomography showing a case of liver metastasis where the right hepatic lobe volume rate decreased from 66.9% to 60.4%. A: Before portal vein ligation (PVL) [right hepatic lobe (RHL) volume rate: 66.9%]; B: After PVL (RHL volume rate: 60.4%); C: The right portal branch was intraoperatively ligated (arrow).

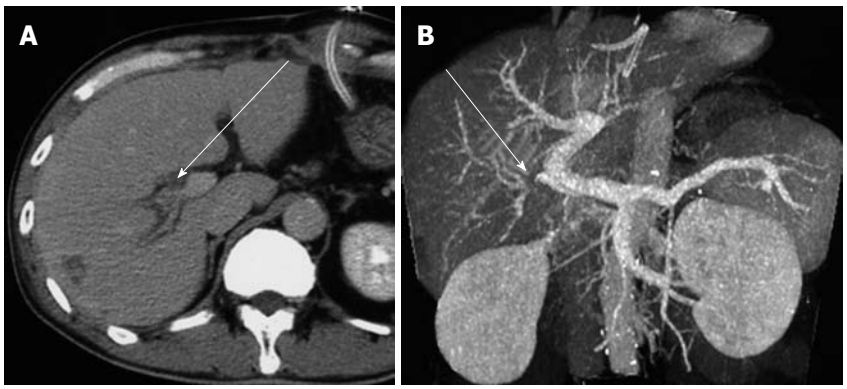

Figure 3 Postoperative computed tomography confirming a degree of residual portal venous flow from the periphery to the ligation point (arrow). A: Axial image; B: Multiplanar reconstruction image.

tion or ablation is performed on the FRL, and PVL is subsequently performed to induce atrophy in the hemiliver to be resected, in preparation for the planned major hepatectomy[17-20]. PTPE has been advocated as a technique for inducing atrophy of the ipsilateral liver without the need for a laparotomy, and is commonly performed for cases such as hilar bile duct carcinoma and hepatocellular carcinoma, in which a substantial liver volume is planned for resection[21-23]. Although PVL and PTPE are both techniques that occlude the portal vein, they differ in approach. PTPE is performed by percutaneously injecting embolic materials, whereas PVL is performed by a laparotomy to ligate the first-order branch of the portal vein. To date, several studies have demonstrated the safety and effectiveness of the two techniques individually; however, there are not enough data available from comparative studies reporting the relative efficacies of the two techniques. In the present study, we compared the atrophic effect and postoperative hepatic hemodynamics associated with PTPE and PVL.

In our study, the PTPE group demonstrated a significantly higher rate of postoperative liver volume atrophy than the PVL group 1 mo after hepatectomy. The mean liver volume atrophy rate was 14.3% ± 2.3% in the PTPE group and 5.4% ± 1.6% in the PVL group (Figures 1 and 2). The CT and Doppler ultrasound findings may explain the reason for this difference. It was confirmed that portal venous flow was completely occluded due to the use of embolic materials acting throughout the peripheral portal vein in the PTPE group. However, portal vein venous flow continued at peripheral sites away from the ligation point in two cases in the PVL group (Figure 3). Residual flow was observed from the anterior to the posterior branch (Figure 4).

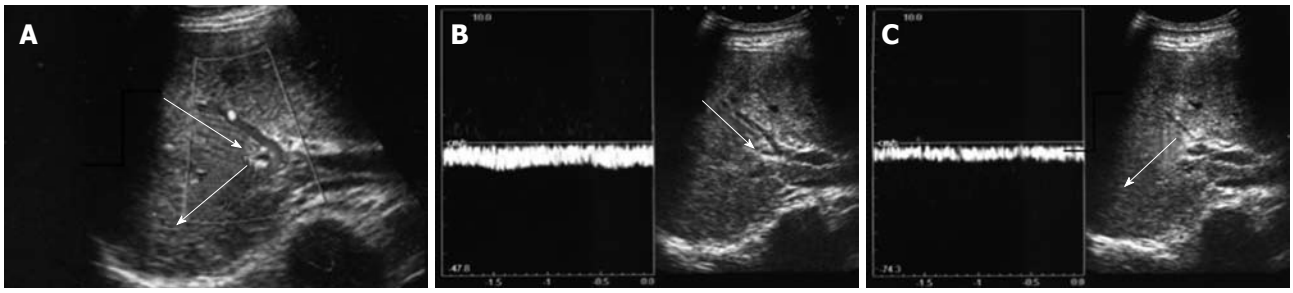

Figure 4 Doppler ultrasound findings on hemodynamics. A: Color Doppler ultrasound confirming portal venous flow from the anterior to the posterior branch (arrow); B: Pulse Doppler ultrasound confirming hepatofugal venous flow in the anterior branch (arrow); C: Pulse Doppler ultrasound confirming hepatopetal venous flow in the posterior branch (arrow).

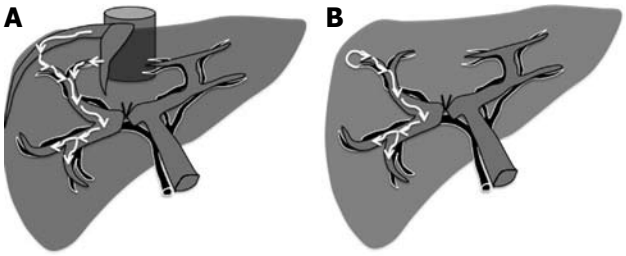

Figure 5 Hemodynamics during portal vein ligation procedure. A: The residual portal venous flow may be explained as backflow from the hepatic vein; B: The presence of an arterioportal shunt may be another reason for the residual portal venous flow.

Two explanations can be proposed for the peripheral portal blood flow observed despite the portal vein being ligated at its central site. First, the observed peripheral portal blood flow could be backflow from the ipsilateral hepatic vein (Figure 5A). Normally, portal vein pressure and hepatic venous pressure are approximately equal at 100-150 mmH_2O. However, ligating the first-order branch of the portal vein may decrease peripheral portal vein pressure, causing a relative pressure elevation in the hepatic vein and resulting in backflow from the hepatic vein. This backflow was significant for cases where tumors had compressed or obstructed hepatic veins in the presence of high hepatic venous pressure. A second possible explanation for the observed peripheral portal blood flow is related to the arterioportal shunt (AP shunt) (Figure 5B). Blood inflow *via* the AP shunt diminishes the effectiveness of the technique by allowing some blood to flow in the first-order branch of the portal vein. Consequently, when the AP shunt is preoperatively observed, PVL should not be the preferred treatment option.

In contrast to the PVL group, postoperative CT data confirmed the presence of embolic materials in the peripheral portal vein in all PTPE patients. In addition, postoperative Doppler ultrasound showed no residual blood in the portal vein, leading us to conclude the superiority of PTPE over PVL. However, PVL is currently more often performed in TSHP cases requiring portal vein occlusion. Time between the first stage and PTPE should be minimized because of possible cancer progression[24,25]. Therefore, we recommend PTPE for the first part of TSHP.

In conclusion, the small sample size and the retrospective nature of this study are limitations towards obtaining more conclusive results, compared to a prospective study with a larger population. However, our results show that PTPE can more effectively and rapidly achieve atrophy of ipsilateral liver volume and consequently induce compensatory FLR volume hypertrophy, compared with PVL.

COMMENTS

Background

Postoperative liver failure may be induced because of the insufficient remnant liver volume after major hepatectomy where more than 60%-70% of the total liver volume is resected in such cases as hilar bile duct carcinoma or liver metastasis. To achieve safer major hepatectomy, ligation or embolization of the portal vein is preliminarily performed to induce atrophy of the ipsilateral liver and hypertrophy of the future remnant liver.

Research frontiers

To occlude unilateral portal vein, either portal vein ligation (PVL) ligating the unilateral portal vein or percutaneous transhepatic portal vein embolization (PTPE) injecting embolic agent to the unilateral portal vein through catheter is performed. PTPE is a procedure advocated after PVL, and PVL cases have decreased in number since the introduction of PTPE. However, as two-stage hepatectomy procedure (TSHP) for liver metastasis has recently become a more popular procedure, PVL has been again increasingly performed in combination with the first resection of TSHP.

Innovations and breakthroughs

The liver atrophy rate of unilateral lobe was compared between the PTPE (n = 9) and PVL groups (n = 4) 1 mo after each procedure. The liver atrophy rate was 14.3% ± 2.3% (PTPE) and 5.4% ± 1.6% (PVL), which was a significant difference (P = 0.0061). To date, the two procedures have been regarded equivalent in effectiveness, however, the results suggest the superiority of PTPE over PVL, and to the best of knowledge, this is the first report to demonstrate such difference.

Terminology

PVL is a procedure to ligate the unilateral portal vein to induce ipsilateral liver atrophy and consequent hypertrophy of the contralateral liver. PTPE is a procedure to occlude the unilateral portal vein by percutaneously injecting embolic agent to induce ipsilateral liver atrophy and consequent hypertrophy of the contralateral liver. TSHP is a surgical strategy adopted for severe metastatic liver cases where it is impossible to remove all malignant lesions in a single procedure. In the first procedure, resectable tumors are removed and after a period of time for liver regeneration, the second procedure is performed to remove the remaining tumors.

Peer review

The current study compared PTPE and unilateral PVL. Using small cohorts, the authors concluded that PTPE is a more effective procedure than PVL as the postoperative liver volume atrophy rate was significantly greater in the PTPE group than the PVL group. This study was novel, well written, technically well conducted, and highly clinically important.

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