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Original article

Percutaneous *ipsilateral* portal vein embolization using histoacryl glue: changing LR, resectibility rate and complications

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Background: Liver resection has been the main strategy for treating either primary or secondary liver cancer. However, major liver resection may lead to postoperative liver failure. Portal vein embolization (PVE) is a procedure to induce hypertrophy of a liver remnant (LR) before major resection surgery. There are many variations in procedural techniques, with different advantages and disadvantages.
Objective: We studied change in liver remnant volume, resectibility rate, and complications after percutaneous *ipsilateral* portal vein embolization (PVE) using histoacryl glue.
Methods: Clinical data of 25 patients who underwent ipsilateral PVE were reviewed. Eighteen patients who had pre- and post- CT studies had total liver volumes (TLV) and LR volumes determined before and after the procedure using MDCT volumetry. Complications and respectability rates were recorded.
Results: All 18 patients who had pre-CT and post-CT studies had increased LR volumes. The mean of LR volumes before and after ipsilateral PVE were calculated at about 449 ml and 586 ml, which were statistically significant (p <0.001). The mean enlargement of LR was 30% (range 4 to 120%). There were no deaths or serious complications. The resectabilty rate was 76%.
Conclusion: Percutaneous transhepatic ipsilateral PVE could increase the LR volumes before major hepatic resection. There were no significant complications in our study group.

Keywords: Histoacryl glue, ipsilateral approach, liver cancer treatment, liver remnant, portal vein embolization

Abbreviations:

CT = Computed tomography
LR = Liver remnant; estimated volume in left hepatic lobe after resection
HCC = Hepatocellular carcinoma
ICC = Intraclass correlation coefficient
IVC = Inferior venacava
LPV = Left portal vein
MDCT = Multidector-row computed tomography
MPV = Main portal vein
PV = Portal vein
PVE = Portal vein embolization
Ipsilateral PVE = portal vein approach by percutaneous punctured into right portal vein branches (ipsilateral site to plan liver resection)
TLV = Total liver volumes; measured whole liver volume

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Cancer is one of the most the common causes of death in Thailand [1, 2]. Primary liver cancer is more prevalent common in males (26.3%) [3], followed by cancer of the lung (15.7%), and colorectal cancers (6.9%). In females, however, primary liver cancer is the third most common cancer (9.2%) after cervical and breast cancers [4]. Liver metastasis occurs commonly in primary cancers of colon or breast. Surgical resection of isolated liver metastasis after removal of the primary lesion has a 5-year survival rate of 27 to 37% [5].

Liver resection has been the main strategy for treatment of primary or secondary liver cancer. However, major liver resection may lead to postoperative liver failure due to inadequate liver remnant. To avoid this complication, preoperative PVE is a standard procedure to induce adequate hypertrophy of the LR volume [6].

Many variations of procedural techniques include portal vein approach with embolization. They have different advantages and disadvantages [7, 8]. The advantage of contralateral PVE is that it is easy to approach but it is likely to incur injury to LR and the left portal vein. The ipsilateral approach is not traumatic to LR but more difficult to select and embolize than the contralateral approach.

At our center, histoacryl glue has been used for PVE because it causes permanent embolization without recanalization and is easy to prepare. However, this glue is harder to control than other embolic materials due to its liquidity and rapid-solidification. This study will evaluate outcomes of percutaneous ipsilateral PVE using histoacryl glue in terms of change in liver remnant volume, resectability rate, and complications.

Material and methods

Study patients

Preoperative PVE is indicated when estimated LR volume is less than 25% of normal liver and less than 40% of damaged liver due to associated conditions such as cirrhosis and previous chemotherapy. PVE is indicated prior to major liver resection in patients with inadequate LR. Observational prospective data were collected between January 1, 2009 and October 31, 2010.

Twenty-five patients, who underwent PVE before right hepatectomy or extended hepatectomy and had fully patent portal veins, were recruited into the study.

Seven patients who did not have either pre-embolization multidetector computed tomography (MDCT) or post embolization MDCT were excluded from liver volume measurement. The remaining 18 patients with available pre- and post- embolization MDCT were recruited for liver volume measurement.

All twenty-five patients gave informed consent. The research proposal was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University.

Percutaneous transhepatic PVE technique

The patient was placed in supine position without sedation. A local anesthetic (2% lidocaine hydrochloride) and a mixture of intravenous 25 mg pethidine in 5 ml normal saline were used for pain control. In all patients, the portal venous system was accessed by the use of a percutaneous transhepatic ipsilateral approach. The embolic material was delivered through the right portal vein branch that supplied the region of the liver designated for resection. Histoacryl glue (0.5 ml × 2 to 4 ampule; Aesculap, B BRAUN, USA) was used. Prior to administration, about 6-12 ml of iodized oil (10 ml Lipiodol Ultra-fluid; Guerbet, Aulnay-Sous-Boid, France) was mixed with histoacryl glue to produce radiopacity.

Procedure

Under ultrasonographic and fluoroscopic guidance, the selected portal vein peripheral branch was punctured percutaneously with a 20-gauge BD spinal needle (Becton Dickinson S.A. S. Agustin del Guadalix Madrid, Spain). An Accustick guide wire (0.018" Angiotech PBN MEDICALS., Denmark) was inserted in the portal vein branch through the needle, and an SKATER Introducer set (6-Fr; Angiotech PBN MEDICALS., Denmark) was inserted into the right portal vein. Then, a guidewire (0.035"; Terumo, Tokyo, Japan) was introduced into the portal vein branch through the 5/6-Fr Introducer II sheath (TERUMO Corporation Tokyo, Japan), and a 5-Fr reverse curve angiographic catheter such as Simmons (TERUMO Corporation Tokyo, Japan), MIK (Boston Scientific International, USA), Duck (Boston Scientific International, USA), and Chg C (Boston Scientific International, USA), was inserted into a main portal branch. Digital subtraction portal venography was performed with the use of a 5-Fr reverse curve angiographic catheter placed in the main portal vein to identify variations of the intrahepatic portal tree and patency of portal system. Before embolization, contrast injections into selected right portal vein branches were performed. Histoacryl glue mixed with iodized oil (Lipiodol Ultra-fluid) was injected under fluoroscopic control into each selected portal vein branch in a centripetal direction. Histoacryl glue and lipiodol mixture injection must be performed rapidly. Subsequently, the catheter was removed. A new 5F angiographic catheter was placed in the main portal vein to repeat portal venography. The residual branch of the right portal vein was selected and embolized by the same technique. The section of liver was blocked with remnant histoacryl glue and lipiodol mixture through the lumen of the catheter to prevent intraperitoneal bleeding at the completion of the procedure. The procedure processes is shown in **Figure 1**.

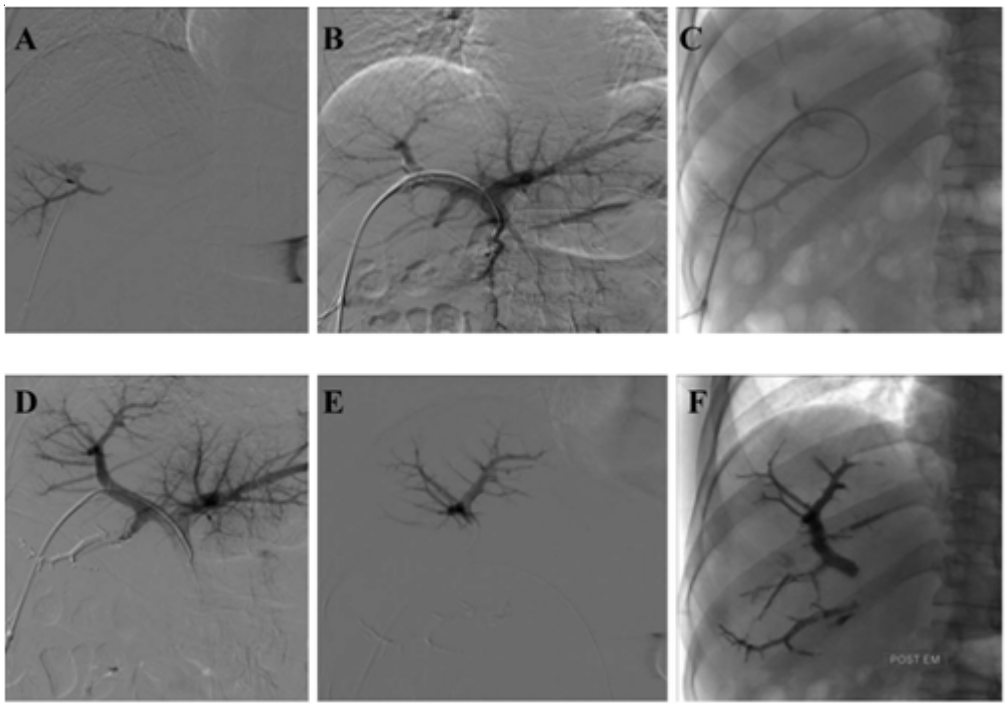

Figure 1. A 48-year-old man with hypervascular liver metastasis showing the transhepatic ipsilateral right PVE technique. **A:** The selected PV peripheral branch was punctured percutaneously and then angiography was performed to confirm tip of needle in portal venous system. **B:** A 5-Fr reverse curve angiographic catheter was inserted into a main portal branch for digital subtraction portal venography to identify variations of the intrahepatic portal tree and patency of portal system. **C:** Before embolization, selective right PV branch contrast injection was also performed. **D:** Histoacryl glue mixed with iodized oil was injected in each selected PV branch, and then the catheter was removed. A new 5F angiographic catheter was placed in main PV to repeat portal venography. **E:** The residual branch of right PV was selected and embolized by the same technique. **F:** Post embolization digital subtraction image at right hepatic lobe shows histoacryl glue occluding right PV branch.

Patient's follow-up

Patients required two to three hours of bed rest after the procedure. The preoperative LR was determined by calculation of total liver volume (TLV) and measurement of the LR (segments I–IV) in cross-sectional imaging before PVE. Post-embolization CT imaging was performed approximately 3 to 4 weeks (mean 24 days) after PVE to determine the degree of liver hypertrophy, as shown in **Figure 2**. The LR/TLV ratio was calculated before and after embolization. Complication and resectability rate after PVE were determined from CT scan.

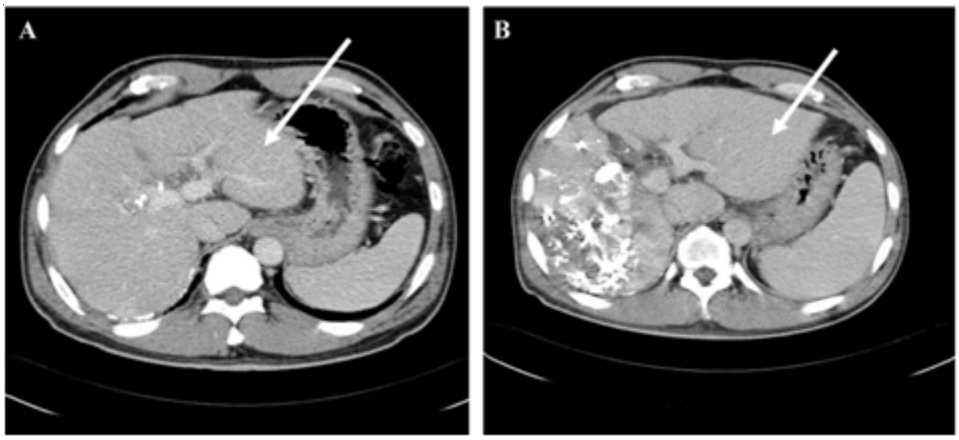

Figure 2. Post contrast enhanced axial CT scan in the same patient. **A**: left hepatic lobe before PVE (arrow) **B**: left hepatic lobe after PVE (arrow).

Measurement of liver remnant

Hepatic volumetric measurements using a multidetector-row computed tomography (MDCT) scanner (SIEMENS medical, Germany) was used to calculate before and after PVE. Serial transverse scans at 5-mm intervals from the dome of the liver to the most inferior part of the liver were obtained and were stored. The volume was calculated by summation of slice volumes using Syngo Volume Evaluation program (version B10/2004A of SIEMENS Medical), giving volume in cubic centimeter. The border of the liver was outline manually using a track-ball excluding gallbladder, IVC, interlobar fissure and PV (**Figure 3**).

Statistics and data analysis

Interobserver reliability in volumetric MDCT measurement was evaluated. Five patients, randomized, were measured by author and study supervisor. Then, the Intraclass correlation power analysis (SPSS analysis software version 16, statistical package for Social Science, Chicago, II) was used for showing agreement. The Intraclass Correlation Coefficient (ICC) close to 0.8-1.0 is considered perfect agreement. In this study, ICC of author and supervisor showed perfectly agreement (ICC = 0.85-1.0).

Quantitative data were expressed as mean, median, and standard deviation using Excel 2007 (Microsoft Corp., Redmond, Wash., USA). The liver remnant (LR) volumes before and after PVE were compared using paired t-test (SPSS analysis software version 16). Factors that determined the increase in LR volume after PVE were analyzed by using Mann-Whitney test (SPSS analysis software version 16). The p-value of ≤ 0.05 is considered statistically significant.

Result

Twenty-five patients were recruited. Eighteen were male and seven were female. Their mean age was 56 years, ranging 40 to 77 years. Five patients had underlying liver damage due to chronic hepatitis B with cirrhosis (n = 4) or previous chemotherapy treatment (n = 1).

Diagnoses were hepatocellular carcinoma (HCC), cholangiocarcinoma, liver metastasis, and hepato-cholangiocarcinoma. Seven patients did not have pre-embolization MDCT or post-embolization MDCT study. These patients were excluded from liver volume measurement. Finally, eighteen patients (HCC n = 6, Cholangiocarcinoma n = 4, and liver metastasis n = 8) were included in liver volume measurement, whereas 25 patients had their complications recorded after ipsilateral PVE and liver resection.

Mean TLV before and after PVE were 1449 ml and 1387 ml, respectively (**Table 1**). Mean LR volume before and after PVE were 449 ml and 586 ml, respectively. Thus, the increased LR volume was 137 ml, which was statistically significant (p <0.001) as shown in **Figure 4**. The calculated ratios of mean LR volume to TLV before and after PVE were 31% and 42%. Thus, the increase of LR volume to TLV was 11%, which was statistical significant (p <0.001). After embolization, mean enlargement of the LR was of 30% (range 4 to 120%) of the pre-embolization volumes, is shown in **Table 1**.

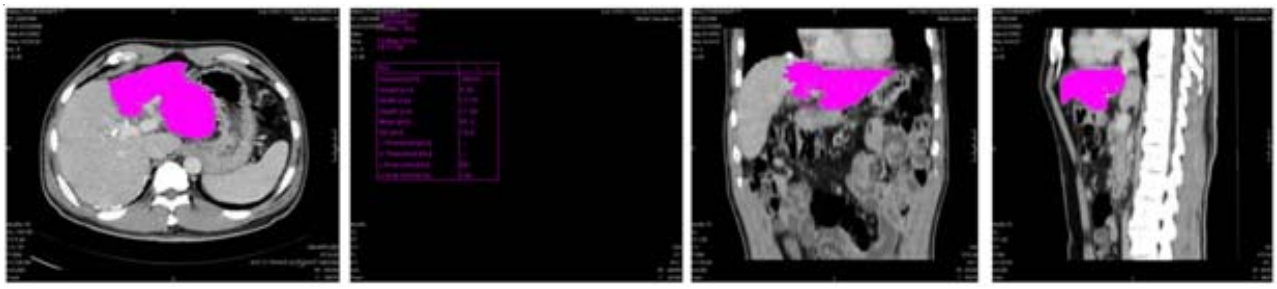

Figure 3. Calculation of the volumes using volume program (Wizard of SIEMENS).

Table 1. Liver volume pre and post PVE

Statistics / Volume	Pre PVE Mean±SD (ml)	Post PVE Mean±SD (ml)	Mean change (ml)	Mean change (%)	*p* value*
TLV	1449±323	1387±293	-62.0	-4.3%	0.27
LR	449±95	586±113	+137	30%	<0.001

*Pair t-test

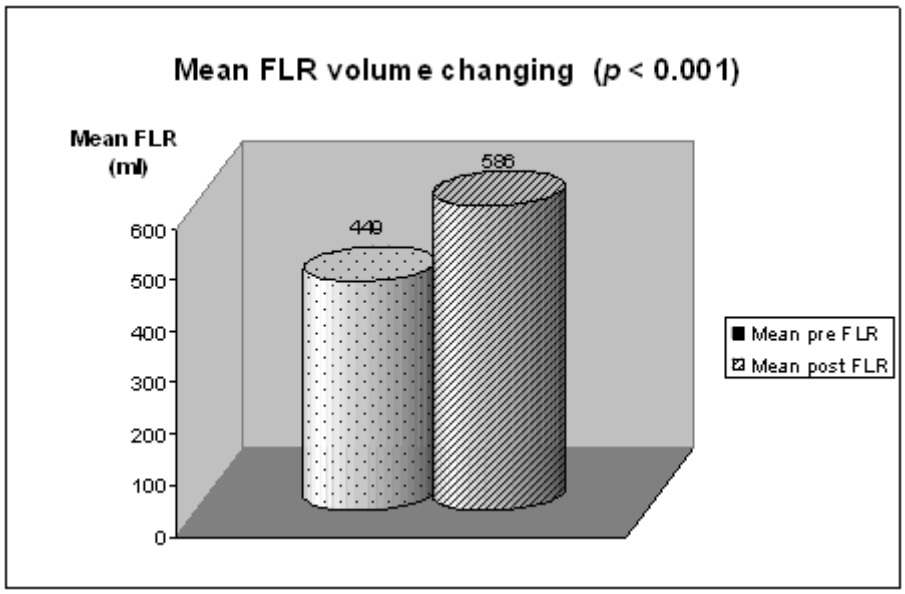

Figure 4. Changing LR volume

Clinical parameters including age, gender, underlying damage to liver such as cirrhosis and previous chemotherapy were studied in relation to the median LR volume. The results are shown in **Table 2**. Younger patients were d"60 years. Median change of LR volume, compared between groups age d"60 years (n = 9) and group age >60 years (n = 9) were 160.14 ml and 111.69 ml, respectively. This was not statistically significant ($p = 0.19$). Male and female patients had the same power of liver regeneration. Median change of LR volumes, compared between males (n = 12) and females (n = 6) were 119.78 ml and 125.43 ml, respectively, which was not statistically significant ($p = 0.89$). Underlying damaged liver also did not significantly affect the enlargement of the LR. Median of LR's volume changes compared between groups with no underlying liver damage (n = 13) and group with underlying liver damage (n = 5) were 132.88 ml and 75.51 ml, respectively, which was not statistically significant ($p = 0.78$).

Complications were recorded in eight patients (32%). One patient had hyperbilirubinemia (TB 5.8). One patient had a partial MPV thrombosis (**Figure 5A**). One patient had partial thrombosis in LPV and hemoperitoneum. One patient had subcapsular hematoma. Two patients had local infection at the puncture site. Finally, two patients suffered from inadvertent glue reflux into the hepatic vein resulting in subsegmental pulmonary artery embolism (**Figure 5B**). All patients with complications showed clinical improvement after conservative treatments and survived.

Table 2. Clinical factors and median increased LR volume

Clinical statistics	Age		Gender		Damage liver	
	≤60	>60	Male	Female	No	Yes
N	9	9	12	6	13	5
Median (ml)	160.14	111.69	119.78	125.43	132.88	75.51
Min (ml)	49.58	15.01	15.01	44.86	44.86	15.01
Max (ml)	414.34	216.93	414.34	160.14	216.93	414.34
p value*	**0.19**		**0.89**		**0.78**	

*Mann-Whitney test

Figure 5. Post contrast CT scan shows partial MPV thrombosis (**A**) and CT scan of another patient shows glue embolism in subsegmental pulmonary artery (**B**)

Follow-up of twenty-five patients was by reviewing operative notes and discharge summaries. Nineteen patients (76%) could undergo hepatectomy. Six patients (24%) could not proceed to surgery due to progression of their disease such as local tumor extension, peritoneal metastasis, or distant metastasis.

The mean volume of glue was 8 ml (range 3 to 12 ml). The mean number of catheters used was two (range 1 to 5 lines). Mean duration of the procedure was 60 minutes (range 20 to 120 minutes).

Discussion

Liver resection is the mainstay strategy for primary or secondary liver cancer. However, major liver resection may lead to postoperative liver failure due to inadequate liver remnant. Portal vein embolization, first reported by Makuuchi et al., is a procedure that can increase LR volume. This study shows a mean enlargement of LR of 30% (range 4 to 120%) after ipsilateral PVE using glue. This is statistically significant (p <0.001). It conforms to results in previous Asian and European studies [9-12].

Differences in race, age, gender, underlying disease, and embolic material may cause differences in increased LR volume from previous reports**.** In the current study, patients in the age group ≤ 60 years, female gender and patient without underlying damaged livers showed higher median LR change than age group >60 years and male patients and those with underlying damage liver, respectively. However, the results were not statistically significant. This may be due to the small number of patients recruited. Therefore, age group, gender, and underlying damage of liver did not influence the power of liver regeneration in this study.

Complications occurred in eight of 25 patients (32%). The result was better than other reports [10, 11, 13, 14]. They were hyperbilirubinemia (TB 5.8), partial MPV thrombosis, pulmonary embolism, partial thrombosis in LPV, and hemoperitoneum. However, all patients that had complications showed clinical improvement after conservative treatments and survived. All patients in this group could proceed to surgery except one due to progression of liver disease. Thus, the resectibilty rate was high, calculated at about 76%. The reasons that prohibited liver resection were local or systemic tumor progression.

Conclusion

Percutaneous transhepatic ipsilateral PVE using glue could increase adequate LR volumes before hepatectomy. No significant complications precluded surgery.

Acknowledgements

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