A novel 2D-perfusion application of a flat-panel detector angiography unit: preliminary experience in preoperative portal vein embolization to predict the change in the remnant liver volume rate

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Aims and objectives

Portal vein embolization (PVE) has been often performed before extended hepatectomy for hilar primary or secondary liver tumors for inducing hypertrophy of the future remnant liver (FRL) as long as curative surgery can be achieved (1-3). Hypertrophy of the FRL is induced by several growth factors such as hepatocyte growth factor (HGF), transforming growth factor (TGF-#), and epidermal growth factor (EGF) derived from the small intestine and carried to the portal vein flow (4, 5). They promote hepatocyte growth in the nonemolized area after PVE (4, 5).

There are several reports about the significant predictors for the hypertrophy of FRL volume rate (FRLR) by PVE such as HGF, TGF, EGF, thymidinkinase, tissue polypeptide antigen, insulin-like growth factor (IGF-1), insulin-like growth factor-binding protein 3 (IGF-BP3), vascular-endothelial growth factor (VEGF), interleukin 2, 6, 8, 10 (IL-2, -6, -8, -10) and tumor necrosis factor # (TNF#) as the serum biomarkers (6). Furthermore, there is an another report that the degree of hypertrophy and growth rate measured by computed tomography (CT) and magnetic resonance imaging (MRI) is the significant predictor of post-hepatectomy liver failure (7). However, to our knowledge, there was no report to predict the effect of PVE during PVE.

Our prototype angiography unit using a flat-panel detector (FPD) in our institution introduced the newly angiography technology so called 2D-perfusion application which could visualize the chronological flow of contrast through vessels as a color coded image. We could evaluated the change of several parameters associated with tissue-perfusion by2D-perfusion application. The purpose of this study was to evaluate the correlation between 2D-perfusion parameter and the change of FRLR.

Methods and materials

Patient population

The institutional review board (IRB) of our institution approved the present study as a retrospective one. Our IRB waved the requirement for written, informed consent for the participation to this study. From June 2011 to September 2013, PVE was performed in 10 patients (7 men, 3 women; median age 68 years, range 51-79 years) prior to their scheduled right or extended hepatectomy (Table 1). Eight patients underwent right portal vein embolization, and the remaining two patients underwent left portal vein
embolization. The underlying diseases were 5 hilar cholangiocarcinomas, 2 intrahepatic cholangiocarcinomas, 1 extensive bile duct cancer, 1 cystic duct cancer, 1 metastatic liver cancer originated from gastrointestinal stromal tumor of stomach. Seven patients underwent an extended right hepatectomy, one did a right hepatectomy and one did a left hepatic trisegmentectomy. One patient underwent PVE and was scheduled for a left hepatic trisegmentectomy but the surgery was canceled because the tumor was suspected for the metastases from the gastric cancer (Table 1). One patient had hepatitis C and another one patient had hepatitis B. All 10 patients had normal liver function without liver cirrhosis (the Child-Pugh score: 5).

MDCT Examination

All ten patients were examined with four-phase contrast-enhanced CT (early arterial, late arterial, portal venous, and equilibrium phase) with a 64-channel MDCT scanner (LightSpeed VCT; GE Healthcare UK Ltd, Buckinghamshire, England) before and 20.8 ± 0.6 days after PVE. Images were reconstructed in a section thickness of 5 mm with 5-mm intervals. Non-ionic contrast material, a bolus of 2 mL/Kg iohexol (300 mg I/mL, Omnipaque 300; Daiichi Pharmaceutical, Tokyo, Japan) was administered intravenously via typically an antecubital vein at a rate of 4 mL/sec with a power injector (Auto Enhance A-60; Nemotokyorindo, Tokyo, Japan). For setting the adequate starting time of hepatic arterial phase scanning, an automatic bolus-tracking program (Smart Prep, GE Healthcare UK Ltd) was used. A circular region of interest (ROI) with an area of 50 pixels was placed in the aorta at the level of the celiac axis. The hepatic early arterial phase scan started automatically 12 s after the threshold enhancement of 50 HU was reached in the aorta with the bolus-tracking program. The late arterial phase scan started 18s after the early arterial phase scan. The portal venous phase scan started 75 s and the equilibrium phase scan started 180 s just after contrast material injection.

CT volumetry and the definition of the change of FRLR

The volumetric data were obtained from the portal phase images. The volumetric MDCT data set was processed on a separate workstation (Advanced Workstation, GE Healthcare UK Ltd, Buckinghamshire, England). The margin of the liver was outlined manually with a computer mouse and the inferior vena cava and the gallbladder were excluded. We defined the border between the right and left liver by the connected line between the middle hepatic vein and the gallbladder. The caudate lobe was calculated as a part of the remnant liver for the unembolized area. The areas of the total liver and the nonembolized portion were measured in each slice of 5 mm in thickness, and then total liver volume (TLV) and FLR were calculated from these data. The change of FRLR increase was calculated as follows; (FRLR after PVE - FRLR before PVE) / FRLR before PVE * 100 (%).
PVE procedure

In all ten patients, PVE was performed under local anesthesia approximately 4 weeks before the scheduled date of their surgery. An Ipsilateral transhepatic percutaneous approach was performed routinely. Under conscious sedation and fluoroscopic control, the left or right branch of the ipsilateral portal vein was punctured under ultrasonographic guidance with an 18 G needle (PTC needle, Create Medic Co, Kanagawa, Japan), and a length of 10 cm and 4 French sheath (Super Sheath, MEDIKIT, Miyazaki, Japan) was inserted. Portography (Figure 1(a)) was performed with a 4-French reverse shaped catheter (FANSAC, Terumo Clinical Supply, Japan) at the main portal vein. The tip of reverse shaped catheter was inserted the origin of the right or left portal vein. Gelatin sponge (Spongel; Yamanouchi, Tokyo, Japan) was used as embolic materials. Approximately gelatin sponge particle was cut in the size of 1-2 mm. The endpoint of PVE was defined until the stasis of embolized portal vein flow (Figure 1(b)). If the catheter tip should be inserted in the more distal position of the segmental portal venous branch, the microcatheter (Nadeshiko swan-neck, JMS, Tokyo, Japan) was used. After embolization, main portal venography was performed to check the embolized lobe and whether the non-target embolization in the contralateral liver lobe was embolized or not. For the embolization of the liver parenchymal access tract, two or three spills with cut gelatin sponge was used to prevent possible intraabdominal hemorrhage. The major and minor complications was evaluated according to Society of Interventional Radiology reporting standards (8).

2D-perfusion application with FPD

The principle of 2D-perfusion application was described elsewhere in detail (9). Our Angiography unit (Allula Xper FD20, Philips Healthcare) can acquire 2D perfusion images based on the dedicated digital subtraction angiography (DSA) images. The specification of acquiring 2D perfusion images were as follows: effective field of view; 25cm × 25cm - 48cm × 48 cm, tube voltage; 120 kV, tube current; 50-325 mA and frame rate; 3 frames per seconds. Injection protocol is a rate of 3 to 4 ml/s with a power injector through the catheter at the main portal vein and the total amount of contrast material 300 mgI/ml (Iomeron, Eizai Co., Ltd.) reaching 12 to 16 mL is used.

The DSA started just after the injection of contrast material. The 2D-perfusion images are acquired before and after PVE in the same acquisition approach like contrast material injection protocol (i.e. amount and rate of contrast material) and the catheter location. The color coded 2D-perfusion image is displayed automatically in about 10 seconds after the data are sent to an equipped workstation (Xtravision; Philips Healthcare).
We selected the whole liver as a circle shaped region of interest (ROI) for the measurement and the time to density curve (TDC) for it is also displayed with the figure of selected parameter to represent the TDC. All the parameters which are calculated in 2D-perfusion application is shown in followings (Figure1C, 1D); i) Arrival time: The Arrival Time is the time between first frames of the frame selection used for processing and the frame where contrast is detected. ii) Mean Transit Time (MTT): The MTT is the time between the Arrival Time and the point of the center of gravity in TDC. This functional parameter is an indication of the average time it takes for contrast to pass through the tissue. iii) Time to peak (TTP): The TTP is the time between the contrast uptake point (the Arrival Time) and the time at which the contrast has maximum density in TDC. iv) Wash-in-rate (WIR): The WIR is defined by the slope of the uptake curve. v) Width: The Width is measured between the inflection points on the wash-in curve and wash-out curve. vi) Area under the curve (AUC): The AUC is the area under the curve between the Arrival Time and the point in TDC, that the contrast has left the vessel. Especially, WIR is considered as the blood flow velocity in the parameters of 2D Perfusion.

We calculated the WIR for the remnant liver parenchyma per unit to compare the WIR before and after PVE. The WIR for the remnant liver parenchyma per unit was defined as follows; WIR for the remnant liver parenchyma per unit before PVE = WIR before PVE / TLV, WIR for the remnant liver parenchyma per unit after PVE = WIR after PVE / FLR before PVE. The change of WIR was calculated as follows; (WIR for the remnant liver parenchyma per unit after PVE - WIR for the remnant liver parenchyma per unit before PVE) / WIR for the remnant liver parenchyma per unit before PVE.

Statistical analysis

Statistical analysis was performed by Statcel statistitical package (Statcel3; OMS Inc., Tokorozawa, Japan). First, the change of FRLR and the change of WIR was evaluated by a test of normality. Second, if the change of FRLR and the change of WIR followed a normal distribution, the correlations between the change of FRLR and the change of WIR was evaluated by Pearson's correlation coefficient. R value was calculated and P value less than 0.05 was considered as a statistically significant difference.

Results

All PVE procedure was successfully performed by contralateral approach in 10 Patients. PVE with the peripheral branches of the left portal vein was performed in 2 patients (20%) including segment IV, whereas PVE with the peripheral branches of the right portal vein
was performed in 8 patients (80%). There were no complications related to the procedure according to Society of Interventional Radiology reporting standards.

FRLR before PVE was 22 to 65% (mean 35.7 ±12%) and FRLR after PVE was 33 to 71% (mean 44.5±10.9%). The change of FRLR was 8.62 to 56.45% (mean 28.1± 16.2%) (Table 2). Difference between FRLR before and after PVE was significant (P= 0.000072)

WIR for the remnant liver parenchyma per unit before PVE was 0.04 to 0.12 (mean 0.078±0.026) and WIR for the remnant liver parenchyma per unit after PVE was 0.12 to 0.44 (mean 0.025±0.09). Difference between WIR for the remnant liver parenchyma per unit before and after PVE was significant (P= 0.00013). The change of WIR for the remnant liver parenchyma per unit: 64 to 468 (mean 230±125) (Table 3). There is positive relationship between the change of WIR for the remnant liver parenchyma per unit and the change of FRLR (R=0.73, p=0.016) (Table 4).

**Conclusion**

Ito F et al, reported that the perioperative morbidity and mortality of the complex biliary and hepatic resections including extended hepatectomy for bile duct cancer were 14 to 76% and 0 to 19%, respectively (10). Postoperative hepatic failure and its associated mortality have been associated with the extent of liver resection (11, 12). Therefore, the preoperative assessment of future liver function after hepatectomy is important whether the extended hepatectomy could be performed or not. There were several reports about the efficacy of preoperative PVE to decrease the perioperative morbidity and mortality (1-4, 13) since Kinoshita H et al. first reported the usefulness of preoperative PVE before the extended hepatectomy (14). The indication for PVE is still controversial yet. But a resection rate of more than 70-75 % of the TLV in normal livers and more than 60-65 % in compromised livers such as liver cirrhosis and fibrosis was mainly the threshold for performing preoperative PVE in most studies (15). The exact mechanism of induction of liver atrophy in embolized area and contralateral liver hypertrophy after PVE are still unknown. The past studies reported that several growth factors such as HGF, TGF, EGF derived from the small intestine via the portal blood flow induced the hypertrophy of the FRL (4, 5). Therefore, the quantitative evaluation of the increase of the portal blood flow could be possible to predict the change of FRLR during PVE. 2D-perfusion application with angiography unit was developed mainly for the evaluation of brain ischemia or acute stroke area during the neurointerventional radiology procedure.

The quantitative evaluation of the portal blood flow could be possible with the values of 2D-perfusion parameters under the same angiography scan protocol and the same
condition of contrast material injection. CT and MRI imaging were reported as the useful modalities for the measurement of liver volume and the evaluation for the degree of hypertrophy of the nonembolized liver (7). But these modalities were mainly performed and evaluated about 3 weeks after PVE. There was no report to predict the effect of PVE during PVE in literature. However, 2D-perfusion application could be performed under PVE and the evaluation for the prediction of the change of FRLR also could be performed by 2D-perfusion application according to the result of our present study. There were several limitations in the present study. First, the present study was the retrospective one and smaller number of patients were included. Further investigation with a larger number of patients will be needed. Second, this study was positive correlation between the change of FRLR and WIR. However, this study was not evaluated for the correlation between another parameters such as serum marker and WIR as a predictor of PVE effect. However, in spite of these limitations, we could consider that this preliminary study about the evaluation of the degree of FRLR has clarified the usefulness of the 2D-perfusion application during PVE.

In conclusion, 2D-perfusion application was useful to visualize the change in liver perfusion in PVE. There was the positive correlation between the change of FRLR and WIR for the remnant liver parenchyma per unit. The change of WIR for the remnant liver parenchyma per unit may be applicable as a procedural endpoint to estimate the change of FRLR.

Personal information

Conflicts of Interest

None of the authors personally has identified a potential conflict of interest. This work was supported by a research grant from Philips medical system Japan.

References


