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Running title: Partial portal vein arterialization

Title: Partial portal vein arterialization using right gastroepiploic artery: a novel solution for portal hypoperfusion

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Abbreviations

CT	Computed tomography
ESLW	Estimated standard liver weight
INR	International normalized ratio
PVA	Portal vein arterialization

***To the Editor*:**

Establishing dual arterial and portal inflow is essential for liver transplantation [1]. Inadequate portal inflow compromises graft function and graft survival [2]. Portal hypoperfusion is usually a consequence of spontaneous portosystemic shunt, ligation of which results in improvement of portal inflow [3]. We encountered a patient with portal hypoperfusion, where no significant shunting could be identified. Portal inflow was boosted with incorporating arterial supply using right gastroepiploic artery. The early results were promising.

A 39-year-old man with decompensated alcoholic cirrhosis underwent deceased-donor liver transplantation in June 2017. He had been waitlisted for progressive liver failure with a model for end-stage liver disease score of 20 since March 2017. The baseline international normalized ratio (INR) and platelet count were 1.8 and 152×10^9/L, respectively. His body weight was 77.8 kg and his estimated standard liver weight (ESLW) was 1226 g [4]. Computed tomography (CT) scan at the time of listing showed patent portal vein with no significant ascites or portosystemic shunting (Fig. 1). The spleen measured 11.7 cm.

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Upon exploration the native portal vein was patent. A 1412 g whole graft (115% ESLW) was implanted with conventional approach. Supra-hepatic (3/0 prolene,

continuous) and infra-hepatic inferior vena cava anastomoses (4/0 prolene, continuous) were constructed. Portal vein anastomosis was performed using continuous 6/0 prolene, allowing a 1-cm growth factor. Completion portal inflow measured 2500 mL/min i.e. 180 mL/min/100 g with ultrasonic flowmeter (Optima Flow-QC, Transonic System Inc., Ithaca, NY 14850, USA). Graft celiac trunk was sacrificed for an aneurysmal dilatation of proximal common hepatic artery. Arterial anastomosis was constructed between graft distal common hepatic artery and recipient hepatic artery proper (7/0 prolene, continuous). Biliary reconstruction was via a duct-to-duct anastomosis between graft and recipient common duct (6/0 polydioxanone, posterior continuous, anterior interrupted). The cold ischemic time and recipient warm ischemic time were 296 and 40 minutes, respectively. Explant weighed 1268 g and pathology showed alcoholic cirrhosis. Liver graft biopsy after implantation revealed mild steatosis (< 5%). There was no portal inflammation or hepatocyte apoptosis to suggest ischemia-reperfusion injury.

Initial post-operative course was a smooth recovery with early return of graft function. The INR reached 1.1 on day 3. Protocoled daily duplex showed satisfactory hepatopetal portal flow until day 9, while the portal flow was found to be dramatically diminished. Although graft function remained well (Fig. 2), patient was re-explored to preclude progression to overt portal vein thrombosis. Operative portal flowmetry

confirmed markedly attenuated portal flow measuring 420 mL/min i.e. 30 mL/min/100 g. There was no thrombosis or kinking at portal vein anastomosis. Portal vein was cannulated via inferior mesenteric vein. Portal pressure was 5 mmHg. Portal venogram revealed sluggish portal flow with a small shunting via the coronary vein (Fig. 3A), which was subsequently ligated. Repeated venogram confirmed no residual shunting but portal flow remained weak (Fig. 3B). No proximal shunting was identified over splenic vein or superior mesenteric vein. Outflow obstruction was searched for. Tri-phasic hepatic venous flow was apparent on intra-operative ultrasound. Hepatic vein was punctured and there was no pressure gradient between recipient central venous pressure (6 mmHg) and graft hepatic veins (4 mmHg).

Despite exclusion of anastomotic error, portosystemic shunt and outflow obstruction, portal flow remained weak. The last resort was to augment the portal flow with partial arterialization. 6 cm length of recipient right gastroepiploic artery (1.5 mm) was isolated and anastomosed end-to-end with a side branch of graft portal vein (1.8 mm) using interrupted 9/0 nylon (Fig. 4). Good portal flow (2100 mL/min i.e. 150 mL/min/100 g) was attained upon release of vascular clamp. Portal pressure was 10 mmHg. Completion venogram demonstrated sustainable hepatopetal flow (Fig. 3C). The right gastroepiploic artery coursed over first part of duodenum (Fig. 4). A decompressive Ryle's tube was inserted to avoid disruption of the alignment. It was

removed on day 2 after re-laparotomy. Graft biopsy after reperfusion showed no evidence of graft congestion or ischemia-reperfusion injury.

Patient was monitored with daily duplex ultrasound which confirmed good portal flow. Alanine aminotransferase normalized on day 2 (Fig. 2) and INR returned to 1.1 on day 4 after re-exploration. Immunosuppression was a combination of Tacrolimus and Mycophenolate Mofetil. Patient was discharged on day 14 after second laparotomy. CT scan at week 4 after re-exploration confirmed patent right gastroepiploic artery supporting graft portal inflow (Fig. 5). Portovenogram was performed at week 6 for suspected portal venous anastomosis narrowing on CT. It revealed sustained hepatopetal flow with no portal vein stenosis (Fig. 6). There was no significant portosystemic shunting. At 3 months after transplantation, there was excellent graft function with normal liver enzymes, a bilirubin level of 13 μmol/L and an INR of 1.1. The platelet count was 151 $\times 10^9$/L.

批注 [m2]: According to Fig. 2, ALT does not normalize in POD 2. Please confirm!

In this patient, poor portal flow was not explained by anastomotic error (stricture or alignment) or outflow obstruction. The culprit was an inadequate portal inflow. In the classical situation, portal inflow could be improved with ligation of portosystemic shunt. In this patient, no significant portosystemic shunting was identified. Ligation of a small coronary shunt only resulted in mild improvement. The comparably

large-for-size liver graft (1412 g, 115% of ESLW) could have possibly contributed. The portal inflow was eventually augmented with arterial supply.

Portal vein arterialization (PVA) was first reported by Jiao et al. for portal vein thrombosis after liver resection [5]. It has been utilized for providing alternative portal inflow where extensive splanchnic venous thrombosis was encountered [6,7]. In these situations, there was complete portal flow arterialization as inflow from splanchnic circulation was absent. In contrast, our case illustrated a unique clinical context where native portal inflow was present, though weak i.e. portal hypoperfusion. We described a novel technique of portal inflow modulation by partial portal vein arterialization. The graft portal vein was partially arterialized via a side branch while the native portal inflow from splanchnic circulation was preserved.

The essence of portal flow modulation is a dedicated balance between hyper- and hypoperfusion [8]. In partial PVA, the splanchnic circulation is directly connected to the arterial system. The consequence of portal hyperperfusion becomes two-fold. In the hepatic circulation, graft hyperperfusion predisposes to hepatic artery vasoconstriction and thrombosis [9]. In the portal system, splanchnic hyperperfusion may lead to hypertensive enteropathy and life-threatening gastro-intestinal bleeding. Even in established splanchnic thrombosis, revascularization and troublesome variceal bleeding have been reported after PVA using hepatic artery [6].

The completion portal flow is a function of pre-existing portal inflow, auxiliary arterial inflow and graft outflow capacity. The auxiliary arterial inflow is the adjustable factor in this equation. Therefore, the diameter thus the flow volume of the artery is the essential considerations in partial PVA. The right gastroepiploic artery measured 1.5 mm in diameter and provided a matched augmentation to the portal system. Portal flow modulation was guided by ultrasonic flowmetry and portal manometry [8]. Post-anastomosis portal flow was 2100 mL/min i.e. 150 mL/min/100 g while the portal pressure was 10 mmHg. A physiological value of portal pressure and portal flow is essential to reduce complications from portal hyperperfusion. We are first to report using right gastroepiploic artery as auxiliary portal inflow. Recipient hepatic artery [10] and donor splenic artery [11] have been used for complete PVA, but might over-perfuse an intact portal circulation. Our clinical decision was supported by satisfactory completion portal flow volume and pressure. Question remains on how to predict these resultant parameters before anastomosis. The question could be answered with accumulation of experiences.

This is the first liver graft receiving portal inflow from both intact portal system and auxiliary arterial supply. For complete PVA, Charco et al. [6] reported normal sinusoidal pressure and Erhard et al. [12] reported normal biopsy. Theoretically, excess portal flow to liver graft should be of less concern in partial PVA. Indeed, the

early return of graft function in this patient indicated no significant early graft injury. Graft biopsy immediately after partial PVA showed no significant pathology. Nevertheless, longer follow-up would be necessitated before the effects of partial PVA could be fully understood. Elevated mesenteric pressure and hypertensive enteropathy could be a potential long term problem.

We reported a novel experience of portal flow modulation with partial portal vein arterialization using right gastroepiploic artery as partial portal inflow. We achieved patent portal flow and excellent graft function. In desperate situations of portal hypoperfusion where no portosystemic shunting could be identified, partial PVA is a feasible option to maintain sustainable portal inflow required for graft survival.

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Figure Legends

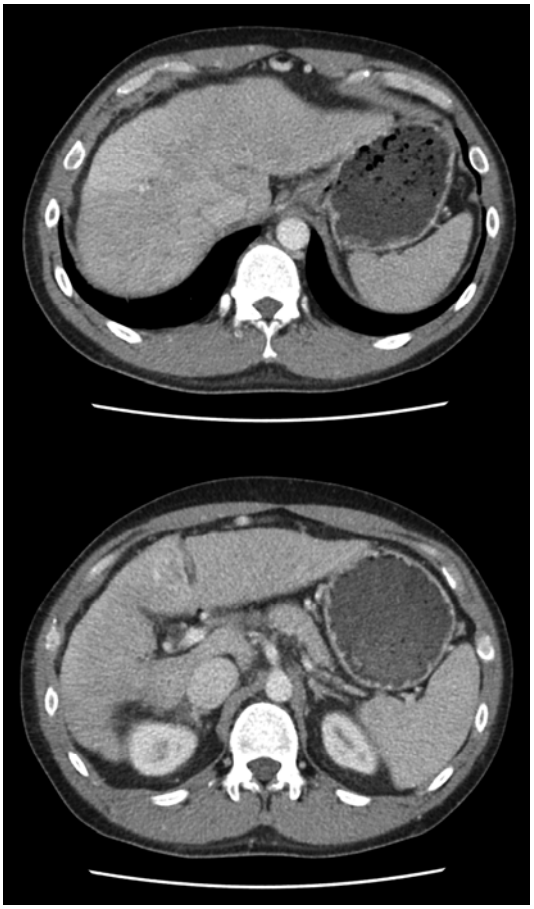


Fig. 1. Preoperative CT scan showing patent portal vein and absence of significant portosystemic shunting.

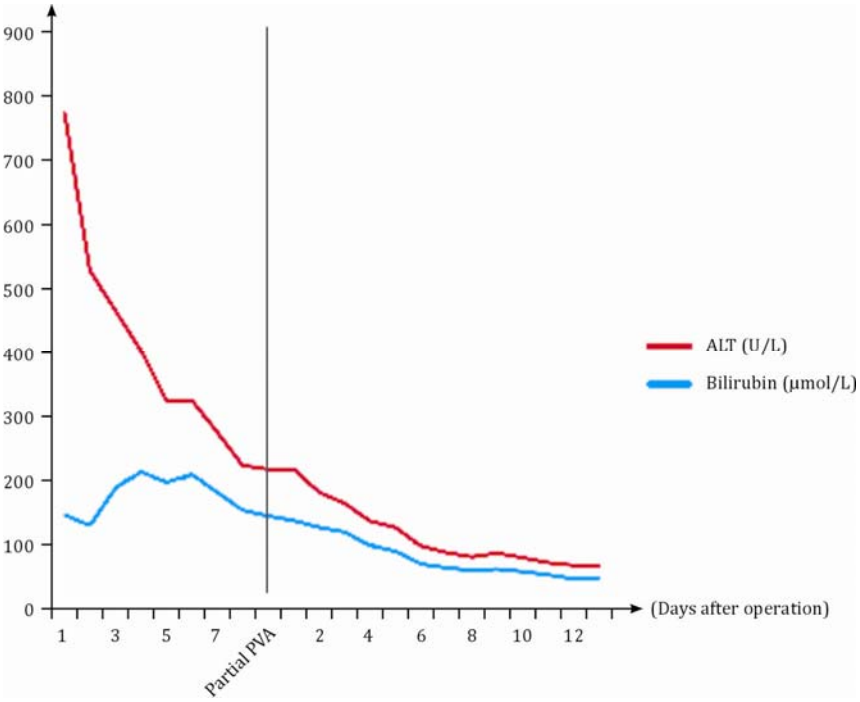
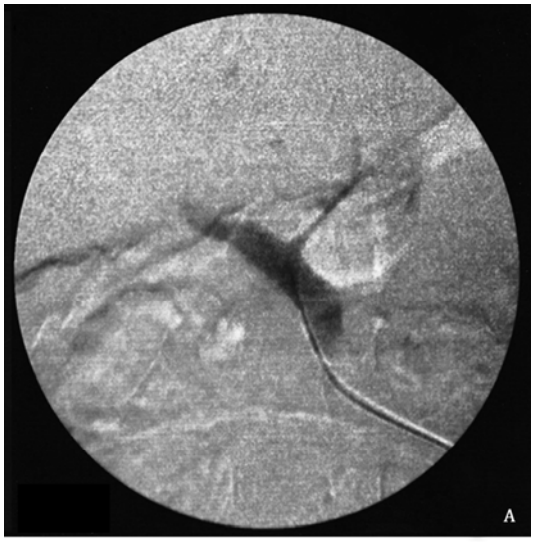


Fig. 2. Graft function after liver transplantation and re-exploration. ALT: alanine transaminase; PVA: portal vein arterilization.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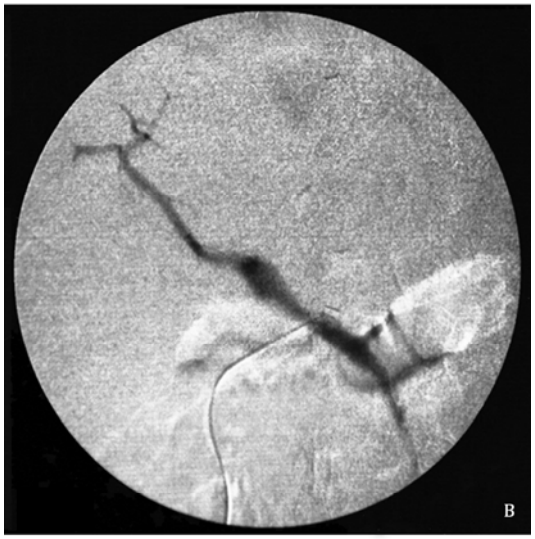
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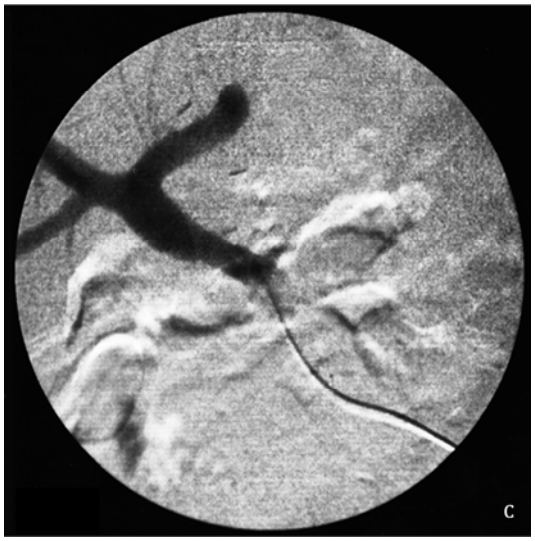
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Fig. 3. Intraoperative portal venogram. **A**: Initial portal venogram revealed sluggish portal flow and a small portosystemic shunt via the coronary vein; **B**: After ligation of the coronary vein, portal flow was visualized but flow remained weak; **C**: After partial arterialization using right gastroepiploic artery, sustainable portal flow to the liver graft was established.

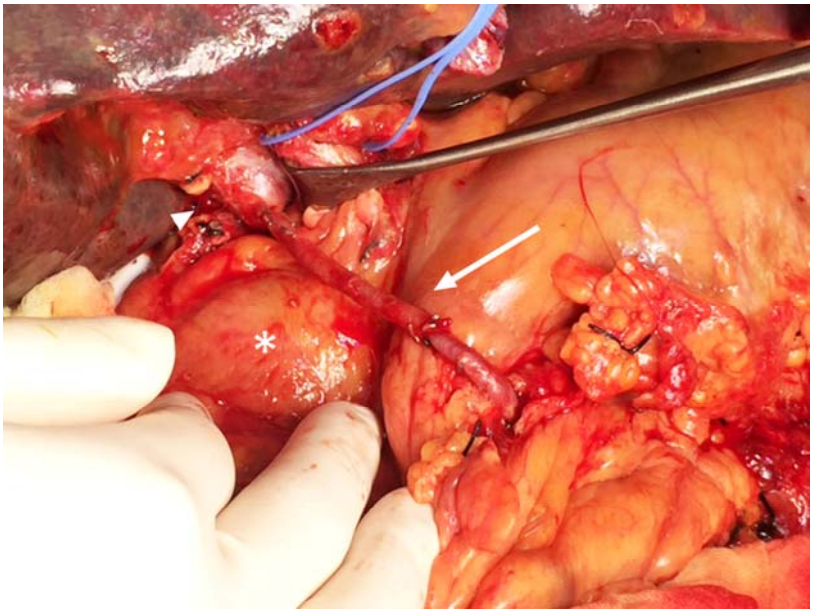

Fig. 4. The right gastroepiploic artery (arrow) was anastomosed to a side branch of the graft portal vein (arrow head). The right gastroepiploic artery coursed over anterior first part of duodenum (*).

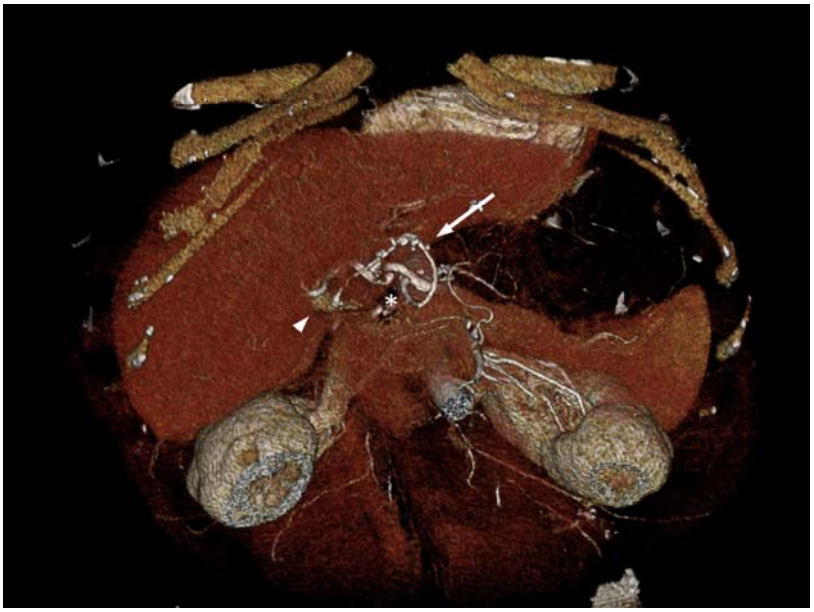

Fig. 5. Reconstructed computed tomography image at week 4 after partial portal vein arterialization showing right gastroepiploic artery (arrow) supporting the portal vein (arrow head). The arterial inflow derived from gastroduodenal artery (*).

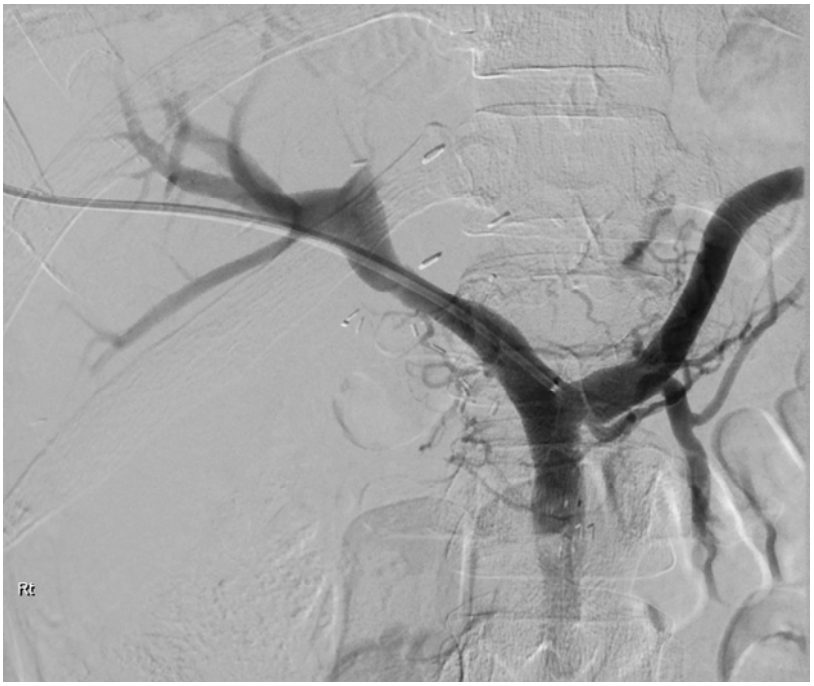

Fig. 6. Portovenogram at week 6 revealed no portal vein stenosis and no significant portosystemic shunting.