Portal vein arterialization as a salvage procedure in hepatopancreatobiliary surgery: a systematic review

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Background: Portal vein arterialization (PVA) is a possible option when hepatic artery reconstruction is impossible during liver resection. The aim of this study was to review the literature on the clinical application of PVA in hepatopancreatobiliary (HPB) surgery.

Methods: We performed a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We systematically searched the PubMed, Embase and Web of Science databases until December 2019. Experimental (animal) studies, review articles and letters were excluded.

Results: Twenty studies involving 57 patients were included. Cholangiocarcinoma was the most common indication for surgery (40 patients [74%]). An end-to-side anastomosis between a celiac trunk branch and the portal vein was the main PVA technique (35 patients [59%]). Portal hypertension was the most common long-term complication (12 patients [21%] after a mean of 4.1 mo). The median follow-up period was 12 (range 1–87) months. The 1-, 3- and 5-year survival rates were 64%, 27% and 20%, respectively.

Conclusion: Portal vein arterialization can be considered as a rescue option to improve the outcome in patients with acute liver de-arterialization when arterial reconstruction is not possible. To prevent portal hypertension and liver injuries due to thrombosis or overarterialization, vessel calibre adjustment and timely closure of the anastomosis should be considered. Further prospective experimental and clinical studies are needed to investigate the potential of this procedure in patients whose liver is suddenly de-arterialized during HPB procedures.

Contexte : L'artérialisation de la veine porte (AVP) est une option envisageable lorsqu'il est impossible de reconstruire l'artère hépatique au moment d'une résection du foie. Le but de cette étude était de faire le point sur la littérature concernant l'application clinique de l'AVP en cours de chirurgie hépatopancréatobiliaire (HPB).

Méthodes : Nous avons procédé à une revue systématique selon les directives PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Nous avons interrogé systématiquement les bases de données PubMed, Embase et Web of Science jusqu'à décembre 2019. Les études expérimentales (chez l'animal), les articles de synthèse et les lettres ont été exclus.

Résultats : Vingt études regroupant 57 patients ont été incluses. Le cholangiocarcinome était la plus fréquente indication de la chirurgie (40 patients [74 %]). L'anastomose terminolatérale d'une branche du tronc cœliaque avec la veine porte a été la principale technique d'AVP (35 patients [59 %]). L'hypertension portale a été la plus fréquente complication (12 patients [21 %] après une moyenne de 4,1 mois). Le suivi médian a été de 12 mois (éventail, 1–87 mois). Les taux de survie moyens à 1, 3 et 5 ans ont été de 64 %, 27 % et 20 %, respectivement.

Conclusion : L'artérialisation de la veine porte peut être considérée comme une option de dernier ressort pour améliorer l'état des patients victimes d'une désartérialisation hépatique aiguë lorsque la reconstruction artérielle est impossible. Pour prévenir l'hypertension portale et les lésions au foie dues à la thrombose ou à l'hyperartérialisation, il faut veiller à ajuster le calibre vasculaire et fermer rapidement l'anastomose. D'autres études expérimentales et cliniques prospectives s'imposent afin d'analyser le potentiel de cette intervention chez les patients dont le foie se trouve subitement désartérialisé durant une chirurgie HPB.

Over the past decade, surgical developments, better patient selection and advances in perioperative management have increased the rate of liver resection for benign and malignant liver lesions.[1,2] Although liver resection is considered the preferred treatment in patients with liver tumours and metastases, only 20% of malignant hepatic lesions are resectable.[3,4] The remaining lesions are often considered unresectable because of lesion numbers, anatomic location of the tumour (with or without vascular invasion) or insufficient remnant liver function.[5] According to data from the US National Cancer Institute, the reported 1- and 5-year overall survival rates for patients with Klatskin tumours are 40.6% and 9.1%, respectively, with a median survival of 7 months.[6] Although these data showed that patients with cholangiocarcinoma who were treated surgically had significantly better outcomes than those who did not undergo surgery,[6] resection, especially of perihilar cholangiocarcinoma, is limited when lesions abut the hepatic artery or when arterial branches of the future remnant liver need to be excised.[7] Moreover, iatrogenic and arterial thrombotic complications in the future remnant liver can influence the postoperative morbidity and mortality rates among patients who undergo liver resection.[8,9]

The hepatic artery carries 25% of blood flow to the liver but supplies 50% of the hepatic oxygen demand.[10] The remaining 75% of blood flow entering the liver is delivered by the portal vein.[11] If the liver becomes suddenly hypoxic owing to resection, thrombosis or iatrogenic injury of the hepatic artery, reconstruction of the hepatic artery is necessary to prevent damage to the intrahepatic biliary tract and subsequent hypoxic liver injury.[8,9,12] If the hepatic artery cannot be reconstructed, arterialization of the portal vein is a rescue option that may improve hepatic inflow and oxygenation of the biliary tract.[13,14] Supplying the de-arterialized liver with arterial blood flow through the portal vein is called portal vein arterialization (PVA).

Initially, PVA was used with the portacaval shunt to reduce postshunt encephalopathy in patients with hepatic cirrhosis and portal hypertension.[15] Later, it was used as a bridge to retransplantation in orthotopic and auxiliary liver transplantation.[14,16,17] In 1992, Iseki and colleagues[18] described a feasible PVA technique in 2 de-arterialized livers during pancreatoduodenectomy and total pancreatectomy. Portal vein arterialization has recently been used as a rescue procedure in hepatopancreatobiliary (HPB) surgery when hepatic artery reconstruction was not possible for oncologic reasons or because of technical limitations.[19,20] In these patients, PVA improved hepatic oxygenation and inflow.[13,14]

The aim of the present study was to perform a systematic review of the literature on the clinical application of PVA as a salvage procedure in HPB surgery.

METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21]

Search strategy

To identify relevant articles published until December 2019, we carried out a systematic search of the PubMed, Embase and Web of Science databases using the following keywords: ("portal vein oxygenation" OR "oxygenation of portal vein" OR "oxygenation of the portal vein" OR "portal vein arterialisation" OR "portal vein arterialization" OR "arterialisation of portal vein" OR "arterialization of portal vein" OR "arterialisation of the portal vein" OR "arterialization of the portal vein" OR "arterio-portal shunt" OR "arterioportal shunt") AND ("liver resection" OR "hepatectomy" OR "trisegmentectomy" OR "lobectomy" OR "segmentectomy" OR "trisectorectomy" OR "hepatic resection" OR "resection of the liver" OR "resection of liver" OR "pancreaticojejunostomy" OR "pancreatectomy" OR "whipple" OR "pancreaticoduodenectomy" OR "duodenopancreatectomy"). We also screened the reference lists of relevant articles for additional eligible studies.

Study selection and data extraction

Two authors (O.G. and E.K.) independently screened all titles and abstracts to identify potentially eligible studies and available full-text articles. All relevant full-text articles were reviewed by A. Majlesara and M.G., who independently appraised the articles, extracted the data and assessed the reliability of the data. Any disagreement was resolved by discussion with the senior authors (K.H., D.-H.C. and A. Mehrabi).

Eligibility criteria

Studies were included according to the following criteria:
- Population: patients who had undergone HPB surgery and PVA
- Intervention: PVA as an alternative or rescue treatment to provide the arterial supply in HPB surgery
- Outcomes: morbidity and mortality
- Study design: all study types that reported intra- or postoperative patient outcomes following HPB surgery with PVA.

To prevent data repetition, we reviewed articles carefully and excluded double publications, review articles, and overlapping and inappropriate reports. In addition, experimental studies including animal subjects were excluded. However, to clarify certain issues, such as pathophysiologic changes after PVA, that, to our

knowledge, have not been investigated in clinical studies, we also reviewed experimental studies.

Quality assessment

Two authors (A. Majlesara and O.G.) assessed the methodologic quality of the included studies independently using the Newcastle–Ottawa Scale and the quality-assessment tool of Murad and colleagues.[22]

Statistical analysis

Outcomes were presented as published originally or were calculated from the reported raw data if possible. Quantitative data were presented descriptively as mean (and standard deviation [SD]) or median values with percentages or ranges. We used the Kaplan–Meier method to analyze 1-, 3- and 5-year survival. Four cases in which follow-up was not reported were excluded from the survival analyses. The statistical analysis was performed with SPSS 25 (StataCorp) for Windows.

RESULTS

The literature search retrieved 306 articles. After duplicate records were excluded, 20 eligible clinical studies that reported the use of PVA in HPB surgery (not including liver transplantation) were identified.[13,14,18–20,23–37] These studies, which were published between 1992 and 2016, were included in the systematic review (Figure 1). The literature review did not identify any prospective studies or randomized controlled trials. Eleven of the included studies were case reports, and 9 were case series with a median sample size of 3.5 (range 2–18). Based on the quality-assessment tool of Murad and colleagues,[22] 15 studies were of good quality,[13,14,18–20,23,25–30,33,34,36] 4 were of intermediate quality,[31,32,35,37] and 1 was of low quality.[24]

A total of 57 patients underwent HPB surgery and PVA. The age and gender of 1 patient,[28] and the age, gender and diagnosis of 3 patients[24] were not mentioned in 2 publications. The remaining 53 patients were aged 33–81 years. Thirty-four patients (64%) were men, and 19 (36%) were women. Most patients (40 [70%]) were diagnosed with cholangiocarcinoma (extrahepatic in 34 and intrahepatic in 6) (Table 1). Forty-six patients (81%) underwent liver resection, 9 patients (16%) underwent pancreatic resection, 1 patient (2%) underwent multiple aneurysm resection, and 1 patient (2%) underwent schwannoma resection (Table 2).

Indications for portal vein arterialization

The reasons for performing PVA during HPB surgery were de-arterialization of the liver owing to excision of

lesions that abutted the hepatic artery (32 patients [56%]), hepatic artery ligation (11 [19%]), hepatic artery thrombosis (6 [10%]), iatrogenic hepatic artery injury (4 [7%]) and failure to reconstruct the hepatic artery after resection (4 [7%]). Portal vein arterialization was performed as primary and secondary salvage surgery in 31 patients (54%) because the hepatic artery was injured or obstructed. In the remaining 26 patients (46%), PVA was reported to be planned because the hepatic artery could not be reconstructed (Table 1).

Surgical techniques

Three different PVA techniques were described in the included studies: use of celiac trunk branches (i.e., common hepatic, gastroduodenal, hepatic and celiac arteries), use of mesenteric vascular branches and use of a jump graft. For use of celiac trunk branches, an end-to-side anastomosis between one of the celiac trunk branches
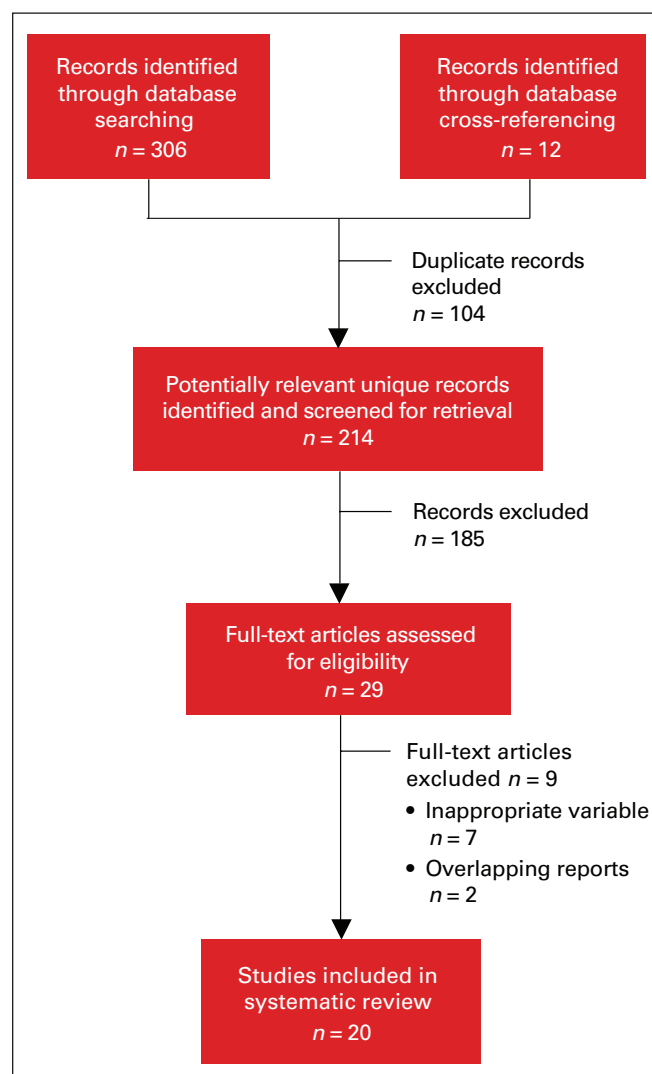

Fig. 1. Flow diagram showing selection of articles for systematic review.

Table 1. Diagnosis, indication and decision time of portal vein arterialization in hepatopancreatobiliary surgery				PVA decision time; no. of patients		
Study and country	No. of patients n = 57	Diagnosis	Indication for PVA	Planned preoperatively n = 26	Primary surgery n = 22	Secondary surgery n = 9
Iseki et al.,[18,19] 1992,1998, Japan	7	ECC (n = 3), pancreatic cancer (n = 2), ICC (n = 1), gallbladder cancer (n = 1)	Lesion excision (n = 3), common hepatic artery ligation (n = 2), hepatic artery thrombosis (n = 2)	2	1	4
Ko et al.,[23] 1995, Japan	1	ECC	Right hepatic artery injury	0	1	0
Ozeki et al.,[24] 1997, Japan	3	NR	Failure of hepatic artery reconstruction (n = 2), proper hepatic artery ligation (n = 1)	0	3	0
Tanabe et al.,[25] 1999, Japan	1	ICC	Hepatic artery thrombosis	0	0	1
Inoue et al.,[26] 2000, Japan	1	ECC	Lesion excision	0	1	0
Teramoto et al.,[27] 2003, Japan	1	ECC	Hepatic artery thrombosis	0	0	1
Fujii et al.,[28] 2007	1	ECC	Failure of hepatic artery reconstruction	0	0	1
Nakamura et al.,[29] 2008, Japan	1	Hilar liver metastasis	Common hepatic artery ligation	0	0	1
Young et al.,[13] 2008, UK	2	ECC	Lesion excision	2	0	0
Chen et al.,[30] 2010, China	4	ECC	Lesion excision	0	4	0
Chen et al.,[31] 2011, China	1	ECC	Lesion excision	1	0	0
Nardo et al.,[32] 2011, Italy	1	Colorectal liver metastasis	Lesion excision	1	0	0
Qiu et al.,[33,34] 2012, 2014, China	4	ECC	Lesion excision	4	0	0
Bhangui et al.,[14] 2014, India	9	Pancreatic cancer (n = 2), ECC (n = 1), ICC (n = 1), gallbladder cancer (n = 1), colorectal liver metastasis (n = 1), celiac trunk aneurysms (n = 1), HCC (n = 1), schwannoma (n = 1)	Lesion excision (n = 4), failure of hepatic artery reconstruction (n = 1), hepatic artery thrombosis (n = 2), hepatic artery injury (n = 1, common hepatic artery ligation (n = 1)	5	3	1
Hokuto et al.,[35] 2015, Japan	1	Colorectal liver metastasis	Hepatic artery injury	0	1	0
Kondo et al.,[20] 2004, and Noji et al.,[36] 2015, Japan	18	ECC (n = 15), ICC (n = 3)	Lesion excision (n = 11), hepatic artery injury (n = 1), hepatic artery ligation (n = 6)	11	7	0
Su et al.,[37] 2016, China	1	Duodenal diffuse large B cell lymphoma	Lesion excision	0	1	0
ECC = extrahepatic cholangiocarcinoma; HCC = hepatocellular carcinoma; ICC = intrahepatic cholangiocarcinoma; NR = not reported; PVA = portal vein arterialization.						

and the portal vein was the main PVA approach (Figure 2A and 2B). The common hepatic artery was used when both the right and left hepatic arteries were resected, and the gastroduodenal artery was used when the left hepatic artery was preserved.[20,36] This method was used in 35 patients (59%) when the hepatic artery was resected because of lesion invasion (Table 2). If possible, an anastomosis should be created between the celiac trunk branches and portal vein initially.[14,20,36] In the included studies, if the celiac trunk branches could not be used because they were obstructed, had a small stump or were lying deep in the hilum, the surgeons performed PVA using the mesenteric vascular branches or an arterial jump graft.[14]

Portal vein arterialization has also been performed by means of an anastomosis between the mesenteric vascular branches (such as the ileocolic, ileal or jejunal artery) and the mesenteric vein branch[14,18,19] (Figure 2C). Portal vein arterialization was performed with this method in 20 patients (34%) following HPB surgery (Table 2). Mesenteric vascular branch anastomosis is a safe procedure in the lower abdominal cavity and leaves the hilum intact for reoperation.[18,19] It was presumed that anastomosis of small mesenteric vascular branches would reduce portal hypertension and related complications because of their smaller calibre (2–5 mm).[19] Although different mesenteric vascular branches (colic, ileocolic, ileal, or jejunal artery and vein) were used, no differences in the effects of these anastomoses were reported.

Portal vein arterialization can also be accomplished with a jump graft between the splenic artery or aorta and the portal trunk via an interposed vascular graft (Figure 2D). Three patients (5%) underwent this

Table 2. Surgical technique and postoperative complications in patients who underwent portal vein arterialization and hepatopancreatobiliary surgery, and cause of death in those who died postoperatively

Study	No. of patients n = 57	Primary operation	PVA technique*†	Postoperative complications‡	No. of deaths n = 22	Cause and timing of death
Iseki et al.,[18,19] 1992, 1998	7§	PD (n = 4), extended right liver resection (n = 2), pancreatectomy (n = 1)	Mesenteric artery (n = 7), splenic artery (n = 1)	Portal hypertension (n = 2), thrombosis (n = 2), liver abscess (n = 1), intra-abdominal bleeding (n = 2)	6	Tumour recurrence (n = 4; 4, 6, 11 and 30 mo), hemorrhagic shock and acute renal failure (n = 1; 8 d), liver failure (n = 1; 41 d)
Ko et al.,[23] 1995	1	Extended left liver resection	Celiac trunk branch	Portal hypertension	0	—
Ozeki et al.,[24] 1997	3	Liver resection	Mesenteric artery	Portal hypertension (n = 1), thrombosis (n = 1), pulmonary disorders (n = 1)	1	Pulmonary edema (in hospital)
Tanabe et al.,[25] 1999	1	Extended left liver resection	Mesenteric artery	Thrombosis	0	—
Inoue et al.,[26] 2000	1	Extended left liver resection	Celiac trunk branch		0	—
Teramoto et al.,[27] 2003	1	PD	Mesenteric artery	Liver abscess	0	—
Fujii et al.,[28] 2007	1	Liver resection	Mesenteric artery	Portal hypertension	1	Tumour recurrence (11 mo)
Nakamura et al.,[29] 2008	1	Liver resection	Mesenteric artery	Portal hypertension	1	Hemorrhagic shock (4 mo)
Young et al.,[13] 2008	2	Liver resection	Celiac trunk branch	Biliary disorders (n = 1), intra-abdominal bleeding (n = 1)	1	Tumour recurrence (23 mo)
Chen et al.,[30] 2010	4	Extended left liver resection	Celiac trunk branch	Liver abscess (n = 1), pulmonary disorders (n = 1)	1	Liver abscess (7 mo)
Chen et al.,[31] 2011	1	Extended left liver resection	NR	Biliary and pulmonary complications	0	—
Nardo et al.,[32] 2011	1	Extended right liver resection	Femoral artery (extracorporeal device)		0	—
Qiu et al.,[33,34] 2012, 2014	4	Liver resection	Celiac trunk branch	Portal hypertension (n = 1), biliary disorders (n = 1), pulmonary disorders (n = 1)	0	—
Bhangui et al.,[14] 2014	9§¶	Liver resection (n = 5), PD (n = 2), resection of celiac trunk aneurysms (n = 1), resection of schwannoma (n = 1)	Mesenteric artery (n = 3), mesenteric vein (n = 3),¶ celiac trunk branch (n = 3), splenic artery (n = 2)	Portal hypertension (n = 3), thrombosis (n = 2), biliary disorders (n = 1), intra-abdominal bleeding (n = 1), liver failure (n = 1)	4	Multiorgan failure (n = 3; 14 and 29 d), unknown (n = 1, 2.5 mo)
Hokuto et al.,[35] 2015	1	Extended liver resection	Celiac trunk branch	Portal hypertension (n = 1), thrombosis (n = 1)	0	—
Kondo,[20] 2004, and Noji et al.,[36] 2015	18	Extended liver resection	Celiac trunk branch	Portal hypertension (n = 1), thrombosis (n = 3), liver abscess (n = 7), biliary disorders (n = 6), intra-abdominal bleeding (n = 3), liver failure (n = 4)	7	Tumour recurrence (n = 3; < 1 yr), upper gastrointestinal bleeding with liver abscess (n = 2; 3 and 9 mo), sepsis with liver abscess (n = 1; 12 mo, sepsis without liver abscess (n = 1; 6 mo)
Su et al.,[37] 2016	1	PD	Celiac trunk branch		0	—

NR = not reported; PD = pancreaticoduodenectomy; PVA = portal vein arterialization.
*Celiac trunk branches include the common hepatic artery, gastroduodenal artery, hepatic artery and celiac artery.
†Mesenteric artery includes the ileocolic artery, ileal artery, jejunal artery and colic artery.
‡Some patients had more than 1 complication.
§PVA was performed twice in 4 patients.
¶Mesenteric vein (middle colic vein, inferior mesenteric vein) was anastomosed to aorta via interposed graft.

procedure (Table 2). Two of these had previously undergone a PVA approach in which mesenteric vascular branch anastomosis was used. In both patients, a second PVA procedure (using the splenic artery) was performed 1 day after the first operation because hepatic ischemia and increased liver enzyme levels indicated a failure of the anastomosis.[14,19] One of the 2 patients had undergone PVA with an anastomosis between the common hepatic artery and portal vein. However, a second PVA procedure (aorta to the middle colic vein with an
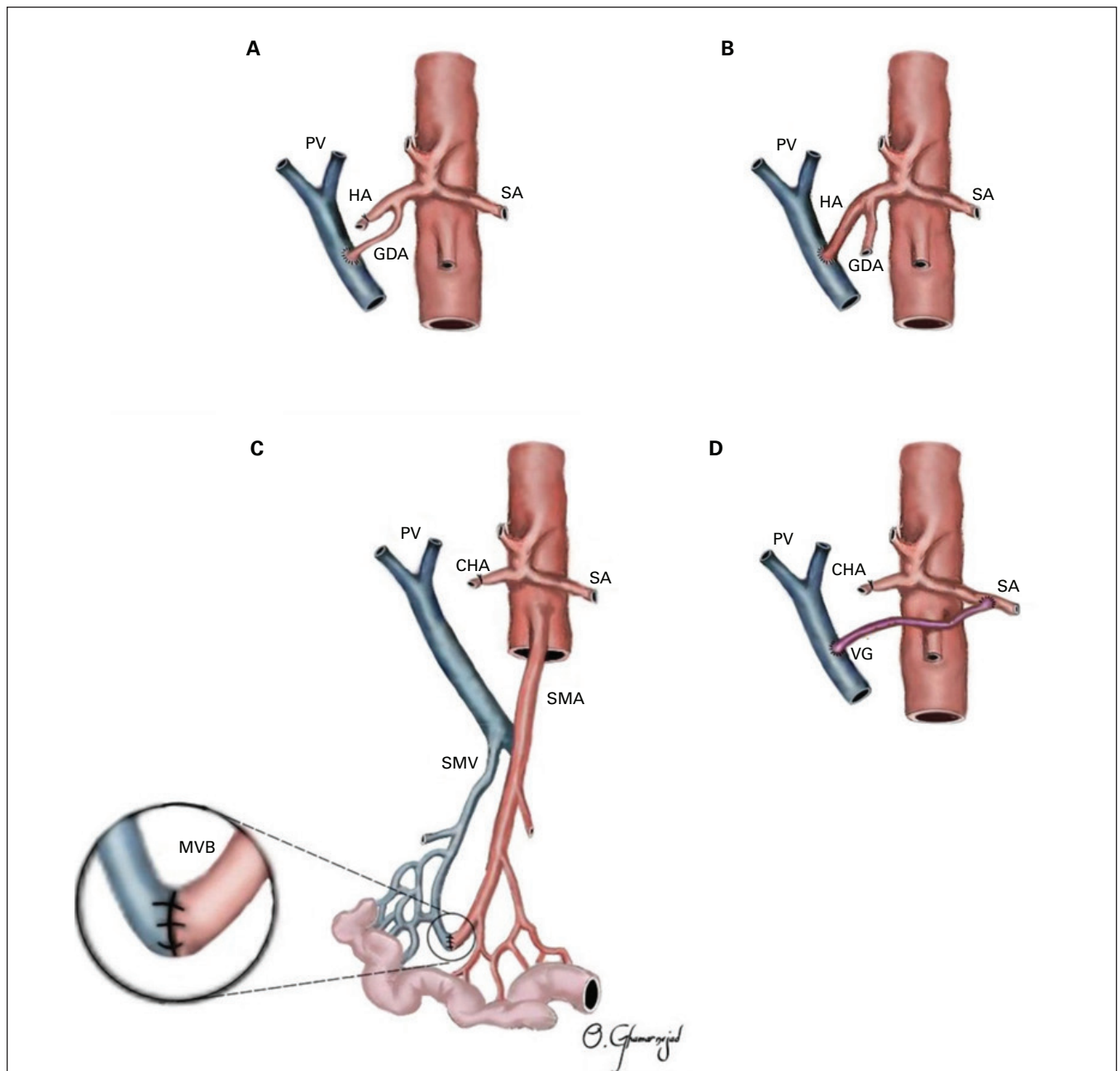
Fig. 2. Different techniques of portal vein (PV) arterialization as an alternative to hepatic artery (HA) reconstruction during hepatopancreatobiliary surgery. (A) End-to-side arterioportal anastomosis between the gastroduodenal artery (GDA) and PV. (B) End-to-side anastomosis between the HA and PV. (C) End-to-end anastomosis between the mesenteric vascular branches (MVBs) when HA reconstruction is not possible because of common hepatic artery (CHA) ligation or injury. (D) End-to-side anastomosis between the splenic artery (SA) and PV via an interposed vascular graft (VG). SMA = superior mesenteric artery; SMV = superior mesenteric vein.

interposition graft) was performed because of PVA thrombosis, which occurred 7 days after HPB surgery.[14]

In addition to the common surgical techniques, Nardo and colleagues[32] introduced an extracorporeal device model for PVA. They interposed this device between the femoral artery and portal vein in a patient who had undergone extended liver resection (Table 2). The device was removed on the seventh postoperative day and the patient was discharged, with an uneventful postoperative course.

Postoperative course and management

Laboratory changes

In the included cases, laboratory analyses revealed a rapid rise in the first 3 days in levels of aspartate aminotransferase (up to 5000 IU/L), alanine aminotransferase (up to 4000 IU/L) and lactate dehydrogenase (up to 11 000 IU/L) in patients who survived after PVA. However, these values gradually decreased until discharge and

had returned to normal at 2 months. Similarly, bilirubin levels increased rapidly early after PVA but declined and plateaued thereafter.[10,19,30,34] None of the studies reported cholestasis parameters such as γ glutamyl transferase and alkaline phosphatase.

Postoperative complications

Early complications: Thrombosis was the most common early complication after PVA, observed in 10 patients (18%) (Table 2). In 9 patients for whom the data were available, the mean time to occurrence of thrombosis was 24.7 (SD 26.9) days (median 20 d, range 2–90 d). Thrombi occurred in celiac trunk branch anastomoses (6 patients [60%]) and mesenteric vascular branch anastomoses (4 [40%]). Thrombosis can be detected early after PVA with routine Doppler ultrasonography.[14] Different therapies have been used to treat PVA-related thrombosis, including anticoagulant therapy and reoperation.[14,35] Bhangui and colleagues[14] suggested that a second PVA procedure should be performed if no arterial collateral flow to the liver is observed, and that no further intervention is required if collaterals are present.

Other early complications observed were biliary disorders (biliary leakage and biliary fistula) (10 patients [18%]), intra-abdominal bleeding (7 [12%]), pulmonary disorders (pulmonary edema, pneumonia and pleural effusion) (4 [7%]) and liver failure (6 [10%]) (Table 2).

Long-term complications: The most common long-term PVA-related complication was portal hypertension, reported in 12 patients (21%) (Table 2). The mean time to occurrence of portal hypertension was 4.1 (SD 3.1) months (median 3 mo, range 1–11 mo). Anastomosis of small mesenteric vascular branches was expected to reduce portal hypertension,[19] but this complication occurred in 7 (35%) of 20 patients with mesenteric vascular branch anastomosis and in 5 (14%) of 35 patients with celiac trunk branch anastomosis.

To prevent portal hypertension and related complications, some authors have recommended restriction of the portal vein calibre by artificial PVA banding.[30,38] In the included studies, 4 patients (7%) underwent PVA involving the hepatic artery, whose calibre was restricted with a silicon tube (about 2 mm in diameter).[30] These patients were followed for 7 months to 1 year without any sign of portal hypertension or related complications.

Closure of the anastomosis has been recommended if portal hypertension occurs postoperatively.[19,23] However, some surgeons performed this as a prophylactic procedure to prevent increased portal vein pressure.[20,36] In 26 (74%) of 35 patients who were still alive during follow-up, the anastomosis was closed by means of coil embolization 4–6 weeks after PVA or occluded spontaneously. Portal hypertension occurred in 8 (35%) of 23 patients in whom PVA was not prophylactic or the anastomosis was closed or occluded, who survived for more than 4–6 weeks. None-theless, the ideal time of anastomosis closure is unknown because long-term studies are lacking. The re-arterialized liver needs adequate time to regenerate without injuries. With this intention, some authors have suggested that the anastomosis be closed 4–6 weeks after surgery if hepatopetal arterial collaterals are observed on angiography.[13,20]

Another long-term complication after PVA was liver abscess, which was reported in 10 patients (18%). Among the 5 patients for whom data were available, this complication occurred 6.4 (SD 4.5) months (median 7 mo, range 1–12 mo) after surgery.

Patient survival

Twenty-two patients died after a median follow-up duration of 12 (range 1–87) months. The cause of death was hemorrhagic shock in 4 patients (18%), pulmonary edema in 1 (4%), multiorgan failure in 3 (14%), liver failure in 1 (4%), postoperative infection (i.e., sepsis and liver abscess) in 3 (14%) and tumour recurrence in 9 (41%); in 1 case the cause was unknown (Table 2). The timing of death is shown in Table 2. The 30- and 90-day in-hospital mortality rates were 7.0% and 14.0%, respectively. Kaplan–Meier analysis showed that the 1-, 3- and 5-year survival rates were 64%, 27% and 20%, respectively.

Pathophysiologic changes after portal vein arterialization

To our knowledge, pathophysiologic liver changes have not been investigated after PVA in clinical studies.[39] However, experimental studies have evaluated the effects of PVA with and without liver resection. They showed an obvious increase in portal vein pressure and flow[40,41] after PVA and liver resection in rats. Portal vein arterialization increases portal vein pressure and flow, which increases the rate of posthepatectomy liver failure or small-for-size-and-flow syndrome.[42] Cavallari and colleagues[43] suggested the use of small or restricted-calibre arteries (e.g., the inferior mesenteric artery) for PVA to prevent a major increase in portal vein flow and pressure. Furthermore, PVA results in less hypoxic liver damage than total liver de-arterialization. Interestingly, a mild increase in portal vein flow and pressure triggers regeneration.[44] Higher rates of remnant liver regeneration and hepatocyte proliferation were reported in liver resection in PVA models than in models without arterial supply (control group).[45–49] Moreover, cholestasis, bile duct injury, inflammation, energy state due to elevation in ATP content, hypoxia and hypoxia-associated gene changes were reported to be decreased with PVA compared to liver de-arterialization without reconstruction.[50,51]

The hepatic artery provides the main oxygen supply to the biliary tract.[10] The liver parenchyma and hepatocytes are supplied with oxygen from both the hepatic artery and the portal vein. Therefore, sudden de-arterialization of the

liver damages the biliary tract rather than the parenchyma.[33,35,52,53] Re-arterialization of the liver can directly increase hepatocyte oxygenation by increasing oxygen saturation in the portal vein. The main goal of PVA is to directly prevent bile duct ischemia by restoring the biliary arterial supply after liver de-arterialization. Portal vein arterialization is expected to improve oxygenation of the biliary tree by increasing the oxygen level in blood flowing back through the hepatic sinusoids. Furthermore, PVA may indirectly allow the development of arterial collaterals, which provide more sufficient oxygenated blood to the de-arterialized liver and hypoxic biliary system.[25,36,54] This is supported by the findings of Kondo and colleagues,[20] who reported that arterioportal shunting of the de-arterialized liver increased oxygen saturation in bile ducts from 28% to 57%. This may prevent major postoperative biliary complications in the de-arterialized liver.[30]

The formation of arterial collaterals is common in patients with hepatic artery obstruction. They arise from preexisting vessels, including the inferior phrenic, gastroduodenal and pancreaticoduodenal arteries. They are also seen in patients who have undergone PVA.[55] Hepatopetal arterial collaterals form as a result of enlargement of native vascular channels to improve blood and oxygen supply to regions of the liver where normal blood flow is restricted or interrupted.[56] Collateral vessel formation is induced by several angiogenic factors such as vascular endothelial growth factor, nitric oxide synthase, platelet-derived growth factor and hepatocyte growth factor, and occurs as early as 10 hours after total hepatic artery occlusion.[49,57]

Arterial collateral function after hepatic artery obstruction depends on the location of the occlusion. If the inferior segment of hepatic artery is occluded, collaterals form through both major pathways (extra- and intrahepatic arterial collaterals). If the proximal segment of the hepatic artery is obstructed, intrahepatic translobar collaterals provide flow to the interrupted system.[56] Therefore, formation of hepatopetal arterial collaterals should be a key issue in patients undergoing PVA because of hepatic artery resection or injury or acute thrombosis.[13,14,23,26] In patients with chronic hepatic artery obstruction due to chronic thrombosis or pressure effect of a tumour, collateral arteries may provide sufficient oxygenated blood to the de-arterialized liver.[55,58] In these cases, the liver can tolerate chronic hypoxia. Hu and colleagues[58] showed that hepatic artery reconstruction may not be always required in patients with hilar cholangiocarcinoma with decreased blood flow. However, posthepatectomy liver failure was noted in about 14% of their patients who underwent liver resection without hepatic artery reconstruction.

In patients with acute obstruction or resection of the hepatic artery, there is not enough time for formation of collateral arteries, and, therefore, the liver is more vulnerable to hypoxic damage. In these cases, PVA could be a bridge procedure to allow collateral arterial circulation to develop when hepatic artery reconstruction is not possible. The risk of bile tract ischemia after chronic hepatic artery occlusion is reduced by the formation of collateral circulation, which sufficiently oxygenates the biliary tract.[56] After angiographic confirmation of arterial collaterals (4–6 wk after PVA), the anastomosis should be closed to prevent "over-arterialization" or portal hypertension.[20,36,59] Prolonged overarterialization of the portal vein affects vascular tissue and the liver parenchyma, which can cause necrotizing vasculitis, intimal fibrosis, hyperbilirubinemia, liver fibrosis and abscess formation.[14,54,60–63]

Arterialized animals were reported to have higher hepatocellular apoptosis and parenchymal necrosis than nonarterialized control animals.[49,63] Ott and colleagues[49] found that the proportion of apoptotic cells was significantly higher in pigs that underwent PVA and liver resection than in those that underwent liver resection alone (control group) on postoperative day 7; however, apoptosis gradually increased in the control group and decreased in the PVA group up to day 21. Müller and colleagues[64] observed significantly more fibrosis and severe obliterative portal vein vasculopathy in rats that underwent PVA with an unregulated portal vein flow than in healthy rats at 84 days.

Discussion

In this systematic review, all included studies were case reports or case series, and the majority of studies were of good quality. Portal vein arterialization was needed more often in patients who had undergone liver resection than in those who had undergone pancreatic surgery. Most cases involved patients with cholangiocarcinoma, and most of the patients underwent PVA because the excised lesions abutted the hepatic artery. Celiac trunk branches were most commonly used for PVA.

Portal vein arterialization was associated with substantial morbidity and mortality in the early postoperative period: the 30- and 90-day in-hospital mortality rates were 7.0% and 14.0%, respectively. The 1-, 3- and 5-year survival rates were 64%, 27% and 20%, respectively. In patients who survived, portal hypertension was the most common complication, occurring in 21% of patients after a mean of 4.1 months.

Given these findings, PVA can be considered as a rescue procedure even if some authors have recommended it as an appropriate method to achieve R0 resection in patients with perihilar cholangiocarcinoma.[14,20] Portal vein arterialization was reported to be justified in cases of excision of lesions that abut the hepatic artery, hepatic artery ligation, hepatic artery thrombosis, iatrogenic hepatic artery injury and failure to reconstruct the hepatic artery after resection.

Because of low case numbers, prospective clinical trials might be difficult to conduct, but well-designed experimental studies would help provide deeper insight into the pathophysiologic features, potential and outcomes after PVA.

Limitations

The major limitation of our review is the nature of the studies found on the topic; i.e., case reports and case series with small samples and a short follow-up duration. The lack of prospective studies, insufficient numbers of patients and lack of long-term follow-up after PVA are further limitations. Therefore, the exact pathophysiologic changes and long-term clinical course after PVA are unknown, as are the effects of restriction of the vessel calibre and programmed anastomosis closure on patient outcomes. Since such evaluations may not be possible in human participants owing to the nature of the procedure, further experimental studies are warranted to obtain data in these areas, as well as to define the advantages and disadvantages of different PVA methods.

Conclusion

Portal vein arterialization is a rescue option aimed at improving the outcome in patients with acute liver de-arterialization in whom arterial reconstruction is not possible. To prevent portal hypertension and liver injuries due to thrombosis or overarterialization, adjustment of vessel calibre and timely closure of the anastomosis should be considered. Further prospective experimental and clinical studies are needed to investigate the potential of this procedure in patients whose liver is suddenly de-arterialized during HPB surgical procedures.

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References

1. Poon RT, Fan ST, Lo CM, et al. Improving perioperative outcome expands the role of hepatectomy in management of benign and malignant hepatobiliary diseases: analysis of 1222 consecutive patients from a prospective database. *Ann Surg* 2004;240:698-708.

2. Moulton CA, Gu CS, Law CH, et al. Effect of PET before liver resection on surgical management for colorectal adenocarcinoma metastases: a randomized clinical trial. *JAMA* 2014;311:1863-9.

3. Wicherts DA, de Haas RJ, Adam R. Bringing unresectable liver disease to resection with curative intent. *Eur J Surg Oncol* 2007;33:S42-51.

4. Jones RP, Hamann S, Malik HZ, et al. Defined criteria for resectability improves rates of secondary resection after systemic therapy for liver limited metastatic colorectal cancer. *Eur J Cancer* 2014;50:1590-601.

5. Alberts SR, Horvath WL, Sternfeld WC, et al. Oxaliplatin, fluorouracil, and leucovorin for patients with unresectable liver-only metastases from colorectal cancer: a North Central Cancer Treatment Group phase II study. *J Clin Oncol* 2005;23:9243-9.

6. Sharma P, Yadav S. Demographics, tumor characteristics, treatment, and survival of patients with Klatskin tumors. *Ann Gastroenterol* 2018;31:231-6.

7. Tanaka K, Matsuyama R, Takeda K, et al. Aggressive liver resection including major-vessel resection for colorectal liver metastases. *World J Hepatol* 2009;1:79-89.

8. Belghiti J, Hiramatsu K, Benoist S, et al. Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. *J Am Coll Surg* 2000;191:38-46.

9. Henrion J, Schapira M, Luwaert R, et al. Hypoxic hepatitis: clinical and hemodynamic study in 142 consecutive cases. *Medicine* 2003;82:392-406.

10. Vollmar B, Conzen PF, Kerner T, et al. Blood flow and tissue oxygen pressures of liver and pancreas in rats: effects of volatile anesthetics and of hemorrhage. *Anesth Analg* 1992;75:421-30.

11. Vollmar B, Menger MD. The hepatic microcirculation: mechanistic contributions and therapeutic targets in liver injury and repair. *Physiol Rev* 2009;89:1269-339.

12. Sakuraba M, Miyamoto S, Nagamatsu S, et al. Hepatic artery reconstruction following ablative surgery for hepatobiliary and pancreatic malignancies. *Eur J Surg Oncol* 2012;38:580-5.

13. Young AL, Prasad KR, Adair R, et al. Portal vein arterialization as a salvage procedure during left hepatic trisectionectomy for hilar cholangiocarcinoma. *J Am Coll Surg* 2008;207:e1-6.

14. Bhangui P, Salloum C, Lim C, et al. Portal vein arterialization: a salvage procedure for a totally de-arterialized liver. The Paul Brousse Hospital experience. *HPB (Oxford)* 2014;16:723-38.

15. Otte JB, Reynaert M, De Hemptinne B, et al. Arterialization of the portal vein in conjunction with a therapeutic portacaval shunt. Hemodynamic investigations and results in 75 patients. *Ann Surg* 1982;196:656-63.

16. Sheil AG, Thompson JF, Stephen MS, et al. Donor portal vein arterialization during liver transplantation. *Transplant Proc* 1989;21:2343-4.

17. Erhard J, Lange R, Rauen U, et al. Auxiliary liver transplantation with arterialization of the portal vein for acute hepatic failure. *Transpl Int* 1998;11:266-71.

18. Iseki J, Touyama K, Noie T, et al. Partial portal arterialization for the prevention of massive liver necrosis following extended pancreatobiliary surgery: experience of two cases. *Surg Today* 1992;22:568-71.

19. Iseki J, Noie T, Touyama K, et al. Mesenteric arterioportal shunt after hepatic artery interruption. *Surgery* 1998;123:58-66.

20. Kondo S, Hirano S, Ambo Y, et al. Arterioportal shunting as an alternative to microvascular reconstruction after hepatic artery resection. *Br J Surg* 2004;91:248-51.

21. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;151:264-9.

22. Murad MH, Sultan S, Haffar S, et al. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med* 2018;23:60-3.

23. Ko S, Nakajima Y, Kanehiro H, et al. Successful management of portal hypertension following artificial arterioportal shunting: report of a case. *Surg Today* 1995;25:557-9.

24. Ozeki Y, Umemoto T, Tateyama K, et al. Partial portal arterialization for dearterialized liver after hepatectomy. *Br J Surg* 1997;84:1011.

25. Tanabe G, Kawaida K, Hamanoue M, et al. Treatment for accidental occlusion of the hepatic artery after hepatic resection: report of two cases *Surg Today* 1999;29:268-72.

26. Inoue T, Sawa T, Okada S, et al. Partial portal arterialization in complete en bloc resection of the hepatoduodenal ligament and left lobe of the liver for hepatic hilar cancer. *Hepatogastroenterology* 2000;47: 533-6.

27. Teramoto K, Kawamura T, Takamatsu S, et al. A case of hepatic artery embolization and partial arterialization of the portal vein for intraperitoneal hemorrhage after a pancreaticoduodenectomy. *Hepatogastroenterology* 2003;50:1217-9.

28. Fujii Y, Shimada H, Endo I, et al. Management of massive arterial hemorrhage after pancreatobiliary surgery: Does embolotherapy contribute to successful outcome? *J Gastrointest Surg* 2007;11:432-8.

29. Nakamura K, Mitsuyoshi A, Shinkura N, et al. Successful treatment of postoperative acute hepatic artery obstruction with mesenteric arterioportal shunt. *Hepatogastroenterology* 2008;55:1073-6.

30. Chen YL, Huang ZQ, Huang XQ, et al. Effect of arterioportal shunting in radical resection of hilar cholangiocarcinoma. *Chin Med J (Engl)* 2010;123:3217-9.

31. Chen D, Lai JM, Liang LJ, et al. Combination with vascular resection and reconstruction in resection of hilar cholangiocarcinoma [article in Chinese]. *Zhonghua Wai Ke Za Zhi* 2011;49:607-10.

32. Nardo B, Vaccarisi S, Pellegrino V, et al. Extracorporeal portal vein arterialization in man after extended hepatectomy to prevent acute liver failure: a case report. *Transplant Proc* 2011;43:1193-5.

33. Qiu J, Wu H, Prasoon P, et al. Portal vein arterialization in hilar cholangiocarcinoma: one case report and literature review. *Eur J Gastroenterol Hepatol* 2012;24:229-32.

34. Qiu J, Chen S, Pankaj P, et al. Portal vein arterialization as a bridge procedure against acute liver failure after extended hepatectomy for hilar cholangiocarcinoma. *Surg Innov* 2014;21:372-5.

35. Hokuto D, Nomi T, Yamato I, et al. Hepatic artery injury during left hepatic trisectionectomy for colorectal liver metastasis treated by portal vein arterialization. *Int J Surg Case Rep* 2015;13:119-24.

36. Noji T, Tsuchikawa T, Okamura K, et al. Resection and reconstruction of the hepatic artery for advanced perihilar cholangiocarcinoma: result of arterioportal shunting. *J Gastrointest Surg* 2015;19:675-81.

37. Su ZJ, Li WG, Huang JL, et al. Pancreaticoduodenectomy assisted by 3-D visualization reconstruction and portal vein arterialization: a case report (a CARE-compliant article). *Medicine (Baltimore)* 2016;95: e4697.

38. Erhard J, Lange R, Giebler R, et al. Arterialization of the portal vein in orthotopic and auxiliary liver transplantation. A report of three cases. *Transplantation* 1995;60:877-9.

39. Tsivian M, Neri F, Prezzi D, et al. Portal vein arterialization in hepatobiliary surgery and liver transplantation. *Transplant Proc* 2007;39: 1877-8.

40. Shimizu Y, Miyazaki M, Shimizu H, et al. Beneficial effects of arterialization of the portal vein on extended hepatectomy. *Br J Surg* 2000; 87:784-9.

41. Yang W, Koti R, Glantzounis G, et al. Arterialization of the portal vein improves hepatic microcirculation and tissue oxygenation in experimental cirrhosis. *Br J Surg* 2003;90:1232-9.

42. Golriz M, Majlesara A, El Sakka S, et al. Small for size and flow (SFSF) syndrome: an alternative description for posthepatectomy liver failure. *Clin Res Hepatol Gastroenterol* 2016;40:267-75.

43. Cavallari G, Bonaiuto E, Tsivian M, et al. Partial portal vein arterialization in acute liver failure. *Updates Surg* 2014;66:183-7.

44. Golriz M, El Sakka S, Majlesara A, et al. Hepatic hemodynamic changes following stepwise liver resection. *J Gastrointest Surg* 2016; 20:587-94.

45. Chen YL, Chen WB, Wan YY, et al. Effects of partial portal vein arterialization on liver regeneration after hepatectomy in minipigs with obstructive jaundice. *Chin Med J (Engl)* 2012;125:2302-5.

46. Fan YD, Praet M, Van Huysse J, et al. Effects of portal vein arterialization on liver regeneration after partial hepatectomy in the rat. *Liver Transpl* 2002;8:146-52.

47. Zullo A, Cannistra M, Cavallari G, et al. Liver regeneration induced by extracorporeal portal vein arterialization in a swine model of carbon tetrachloride intoxication. *Transplant Proc* 2015;47:2173-5.

48. Niu J, Dong C, Zhang J, et al. TNF-α, HGF and TGF-β1 are involved in liver regeneration following partial hepatectomy using portal vein arterializations. *J Med Biochem* 2012;31:135-9.

49. Ott R, Schuppan D, Tannapfel A, et al. Portal vein arterialisation as a technical option in liver transplantation: impact on function, regeneration, and morphology of the liver following hemihepatectomy in pigs. *Liver Int* 2003;23:54-62.

50. Jiang J, Wei J, Wu J, et al. Partial portal vein arterialization attenuates acute bile duct injury induced by hepatic dearterialization in a rat model. *Biomed Res Int* 2016;2016:7427246.

51. Li DZ, Jiang J, Miao Y. Cholangiocytes of cirrhotic rats are more tolerant to ischemia than normal rats: A role for abnormal hepatic arteriovenous communications? *J Surg Res* 2011;169:e167-74.

52. Tsuge H, Mimura H, Hamazaki K, et al. Interruption of hepatic arterial blood flow after resection of pancreaticobiliary carcinoma. *Hepatogastroenterology* 1995;42:966-74.

53. Gupta N, Solomon H, Fairchild R, et al. Management and outcome of patients with combined bile duct and hepatic artery injuries. *Arch Surg* 1998;133:176-81.

54. Hidalgo E. Portal vein arterialization: 'enjoy' it responsibly. *HPB (Oxford)* 2014;16:739.

55. Vaidya S, Dighe M, Bhargava P, et al. Chronic hepatic artery occlusion with collateral formation: imaging findings and outcomes. *Transplant Proc* 2011;43:1770-6.

56. Mays ET, Wheeler CS. Demonstration of collateral arterial flow after interruption of hepatic arteries in man. *N Engl J Med* 1974;290: 993-6.

57. Carmeliet P, Jain RK. Angiogenesis in cancer and other diseases. *Nature* 2000;407:249-57.

58. Hu HJ, Jin YW, Zhou RX, et al. Hepatic artery resection for bismuth type III and IV hilar cholangiocarcinoma: Is reconstruction always required? *J Gastrointest Surg* 2018;22:1204-12.

59. Yamamoto R, Sugiura T, Okamura Y, et al. Multidisciplinary treatment of left hepatic artery pseudoaneurysm after hepatobiliary resection for gallbladder cancer: a case report. *Surg Case Rep* 2019; 5:192.

60. Charco R, Margarit C, Lopez-Talavera JC, et al. Outcome and hepatic hemodynamics in liver transplant patients with portal vein arterialization. *Am J Transplant* 2001;1:146-51.

61. Ott R, Böhner C, Müller S, et al. Outcome of patients with pre-existing portal vein thrombosis undergoing arterialization of the portal vein during liver transplantation. *Transpl Int* 2003;16:15-20.

62. Müller V, Ott R, Tannapfel A, et al. Arterialization of the portal vein in liver transplantation: a new microsurgical model in the rat. *Transplantation* 2001;71:977-81.

63. Schleimer K, Stippel DL, Kasper HU, et al. Portal vein arterialization increases hepatocellular apoptosis and inhibits liver regeneration. *J Surg Res* 2008;149:250-8.

64. Müller V, Brummer D, Kissler H, et al. Effects of portal vein arterialization on regeneration and morphology in liver transplantation: investigations using the rat model. *Transplantation* 2004;78: 1159-65.