Surgery 165 (2019) 291–297

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Pancreas

Impact of portal vein resection with splenic vein reconstruction after pancreatoduodenectomy on sinistral portal hypertension: Who needs reconstruction?

Masayuki Tanaka, MD, PhD[a], Hiromichi Ito, MD[a,*], Yoshihiro Ono, MD, PhD[a], Kiyoshi Matsueda, MD, PhD[b], Yoshihiro Mise, MD, PhD[a], Takeaki Ishizawa, MD, PhD[a], Yosuke Inoue, MD, PhD[a], Yu Takahashi, MD, PhD[a], Makiko Hiratsuka, MD, PhD[b], Toshiyuki Unno, MD, PhD[b], Akio Saiura, MD, PhD[a,*]

[a] Department of 1Hepato-Biliary-Pancreatic Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan
[b] Department of Diagnostic Imaging, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

ARTICLE INFO

Article history:
Accepted 28 August 2018
Available online 27 September 2018

ABSTRACT

Background: Resection of the porto-mesenterico-splenic confluence is at times necessary during pancreatoduodenectomy with portal vein resection for pancreatic cancer. Although splenic vein ligation can cause sinistral portal hypertension, the incidence of clinically relevant sinistral portal hypertension remains unknown, and the roles of the preservation of potential collateral veins and splenic vein reconstruction are controversial.

Methods: Patients with pancreatic cancer who underwent pancreatoduodenectomy with porto-mesenterico-splenic confluence resection were assessed for incidence of development of varices by computed tomography at 6 months after pancreatoduodenectomy. We evaluated the risk factors for sinistral portal hypertension and the impact of splenic vein reconstruction on sinistral portal hypertension.

Results: Of the 118 patients who underwent pancreatoduodenectomy with porto-mesenterico-splenic confluence resection, 31 (26%) underwent splenic vein reconstruction, 44 patients (37%) developed gastroesophageal varices, and 5 (11%) experienced varix rupture. Sacrifice of all 3 potential collateral veins (what we refer to as the critical veins: left gastric vein, middle colic vein, and superior right colic vein arcade) and absence of any spontaneous splenorenal shunt had a substantial impact on formation of varices. The risk of variceal formation could be stratified based on the number of preserved critical veins, and patent splenic vein reconstruction was associated with a decreased incidence of varices (60% versus 100%, $P = .018$) among the patients without preservation of the critical veins. In contrast, patients with multiple intact critical veins developed no varices, regardless of splenic vein reconstruction.

Conclusions: Sinistral portal hypertension is not uncommon after pancreatoduodenectomy with porto-mesenterico-splenic confluence resection, and the number of preserved critical veins helps to predict the risk of sinistral portal hypertension. Thus, the indication for splenic vein reconstruction should be tailored according to individual risk factors.

Introduction

Although pancreatoduodenectomy (PD) with en bloc portal vein (PV) resection is well accepted as a safe and effective operation for patients with pancreatic cancer with PV invasion; management of the splenic vein (SpV), however, remains controversial when the porto-mesenterico-splenic confluence (PMSC) needs to be resected. Some surgeons claim that the SpV can be ligated without any negative consequences and that, therefore, reconstruction is unnecessary.[1,2] In contrast, others recommend SpV reconstruction to prevent the theoretic risk of sinistral portal hypertension (SPH).[3–6]

SPH is a clinical syndrome caused by isolated SpV thrombosis/obstruction, with underlying various etiologies.[7,8] Patients with SPH may present with varices in the gastrointestinal (GI) tract,

* Corresponding authors: Department of Hepato-Biliary-Pancreatic Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research 3-8-31 Ariake, Koto-ku, Tokyo 135-8550, Japan.
E-mail addresses: hiromichi.ito@jfcr.or.jp (H. Ito), akio.saiura@jfcr.or.jp (A. Saiura).

https://doi.org/10.1016/j.surg.2018.08.025
0039-6060/

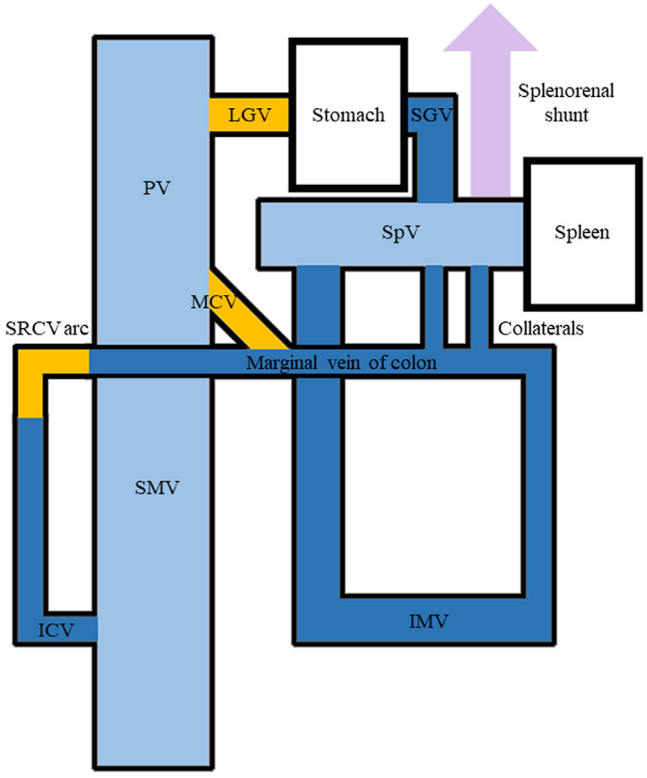

Fig. 1. Venous flow of the splenoportal circulation: three veins (left gastric vein, middle colic vein, and superior right colonic vein arcade) that were suggested previously as potential collateral flows after splenic ligation were designated as critical veins.

usually the stomach and esophagus, with or without splenomegaly, and gastroenteric bleeding with rupture of their varices can be a lethal complication. Although there are multiple case reports of patients with SPH who developed serious GI bleeding,[7,9] the incidence and clinical relevance of SPH among patients who underwent PD with SpV ligation remains unknown.

Strasberg's group conducted meticulous venous mapping by contrast computed tomography (CT) in 15 patients who underwent PD with SpV ligation and demonstrated two major collateral routes that developed after SpV ligation—the superior route via the left gastric vein (LGV) and the inferior route via either the right colonic marginal vein arcade (SRCV arc) or the middle colic vein (MCV), draining into the superior mesenteric vein.[10,11] Consequently, they speculated that these collateral veins could protect similarly treated patients from developing SPH.[10,11] Our earlier evaluation of 43 patients after PD with SpV ligation similarly demonstrated that sacrificing the SRCV arc was associated with postoperative varix formation.[12] It is important to note that these potential collateral veins, including the LGV, MCV, and SRCV arc, often need to be sacrificed for oncologic clearance. Based on these observations, we designated these three veins as critical veins for the development of collateral flow (Fig 1). We hypothesized that the risk of SPH after PD with SpV ligation could be predicted according to the number of preserved critical veins and that the management of SpV should be tailored depending on the risk of SPH for each individual patient.

This study, therefore, aimed to address the incidence of both SPH and variceal bleeding after PD with SpV ligation among patients with pancreatic cancer, to stratify the risk of SPH according to the number of preserved critical veins, and to evaluate the surgical outcomes of SpV reconstruction and its impact on SPH.

Methods

Study cohort and our approach for patients with pancreatic cancer

This study was approved by the Institutional Review Board (IRB) of the Cancer Institute Hospital (Tokyo, Japan). We reviewed the medical records of consecutive patients who underwent PD for pancreatic adenocarcinoma from January 2009 to December 2016, and those who underwent PD with PV resection and SpV ligation were included. Informed consent was obtained preoperatively from every patient enrolled in this study.

Our approach to managing pancreatic cancer is described elsewhere.[13] In brief, all patients who present with pancreatic cancer are evaluated with preoperative imaging studies, including thin slice, multidetector CT of the chest/abdomen/pelvis and magnetic resonance imaging (MRI) of the liver for preoperative staging. The resectability is determined preoperatively based on the CT imaging according to the guidelines of the National Comprehensive Cancer Network.[14] After January 2015, all patients with borderline resectable tumors received neoadjuvant chemotherapy with gemcitabine and Nab-paclitaxel, followed by operative resection. Before that period, patients with resectable or borderline resectable tumors underwent upfront exploration and resection if possible. After successful recovery from the operation, patients received adjuvant chemotherapy with gemcitabine or S1 and are followed with serial CT every 3 months. None of our patients received radiation therapy either in the adjuvant or neoadjuvant setting.

Operative techniques and management of portomesenteric vein branches

The technical details of our PD have been described elsewhere.[15] Briefly, when the preoperative CT indicates direct tumor contact to the PV, en bloc PV resection is planned. We prefer cylindric, segmental PV resection with primary end-to-end anastomosis over the technique of wedge resection with patch closure, and an interposition graft is rarely used. Depending on the length or location of the PV-tumor contact, the PMSC is resected as necessary. Before December 2013, the stump of the SpV was always ligated, and no reconstruction was performed. Since that period, the splenic drainage route is reconstructed in some patients in various ways according to the surgeon's discretion. The types of reconstruction include splenorenal shunt with end-to-side anastomosis, spleno-gonadal shunt with end-to-end anastomosis, and porto-spleno side-to-end anastomosis with or without an interposition graft (Fig 2). After PV resection with or without SpV reconstruction, no antiplatelet or anticoagulation agents are used prophylactically. In terms of the potential future collateral veins, the LGV is sacrificed almost routinely to facilitate lymphadenectomy around the common hepatic artery and to obtain greater soft tissue margins, with the MCV and inferior mesenteric vein (IMV) also frequently divided. In contrast, the SRCV arc is intentionally preserved unless the tumor involves this area of the mesocolon.[12]

Assessment of sinistral portal hypertension and definitions of collateral veins versus varices

To evaluate SPH, we focused on the GI varices as assessed by thin-slice helical CT with intravenous contrast at 6 months after the operation. Blood flow from the spleen was traced carefully, using serial 1-mm axial slices. Visible veins larger than 1 mm in diameter that were not detectable on preoperative CT were defined as newly formed parts of the venous system, and venous development in the mesentery or omentum was defined as collateral development. In contrast, development of usually gastroesophageal intramural veins was defined as new varicose vein formation and

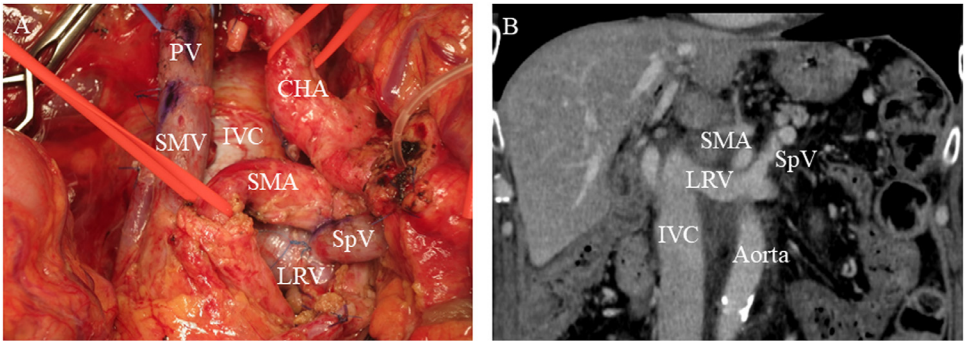

Fig. 2. (*A*) Splenic vein reconstruction: after pancreatoduodenectomy with en bloc resection of the PMSC, the PV, and SMV were anastomosed, and the splenic vein outflow was re-established with a splenorenal shunt. (*B*) Postoperative CT at 6 months showed a patent reconstructed splenic outflow.

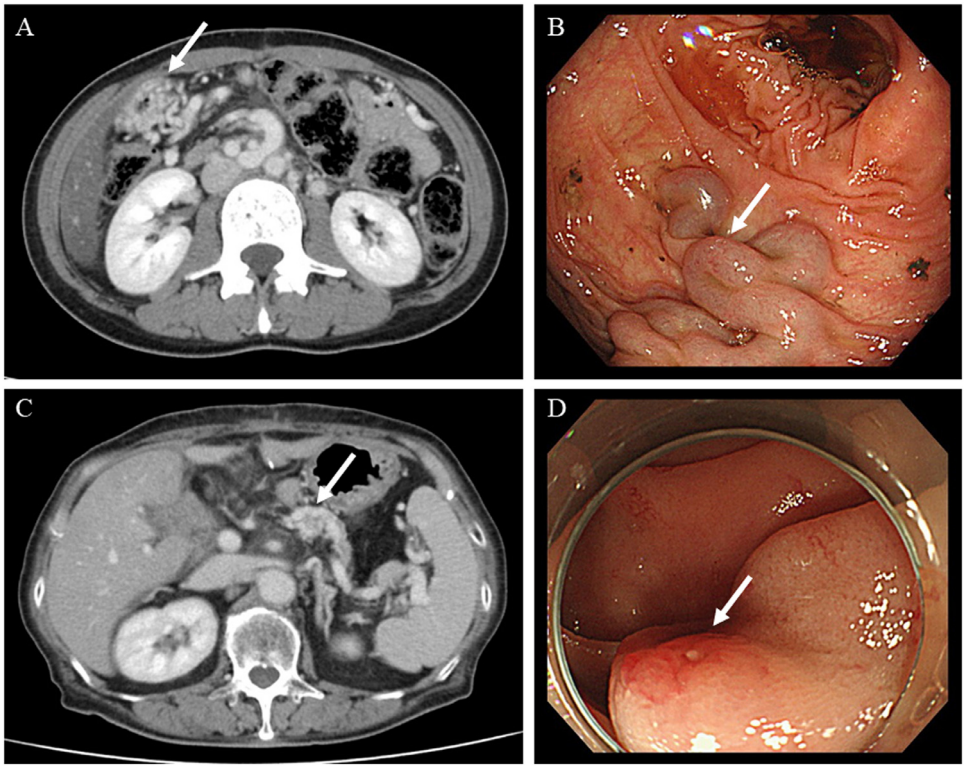

Fig. 3. CT and endoscopic findings for patients with GI varices after pancreaticoduodenectomy. Representative images were shown for (*A, B*) the patient with varices at the hepatic flexure of the colon and (*C, D*) the patient with varices near the pancreaticojejunostomy.

such venous development was diagnosed as SPH (Fig 3). All images were reviewed retrospectively by two experienced gastrointestinal radiologists (M.H. and K.M.).

Earlier works by the Strasberg group and our group suggested the important role of the LGV, MCV, and SRCV arc as collateral routes after SpV ligation.[10–12] Thus, in this study, we designated these three veins as critical veins, and the patency of each critical vein after the operation was evaluated in CT imaging at 6 months after surgery.

Statistical analysis

Categorical variables were compared by either the χ^2 test or the Fisher exact test, and continuous variables were compared, using the Mann-Whitney *U* test. All statistical analyses were performed using R v 3.2.3 (R Project for Statistical Computing, Vienna, Austria).

Results

Incidence of SPH and its complications as a consequence of PD with SpV ligation

Among 333 patients who underwent PD for pancreatic cancer during the study period, 211 patients (63%) underwent PD with PV resection, and 132 of those underwent resection of PMSC with splenic ligation. With 14 patients having inadequate follow-up or missing data, 118 patients were included in the final analysis. Table 1 presents a summary of the demographics of our cohort of patients and the tumor characteristics. In brief, the median patient age was 68 years (range; 37–86 years), and 53% were male. Most patients had advanced tumors with 95% having T3+ and 69% having N1+, 87 patients (74%) had their SpV ligated only, and 31 patients (26%) underwent SpV reconstruction. A spontaneous splenorenal shunt, not detected in the preoperative CT, was evident in 13 patients (11%) in the follow-up CT at 6 months. Among

Table 1
Patient demographics and tumor characteristics.

		Total $n = 118$
Age, years; median (range)		68 (37-86)
Male sex, *n* (%)		63 (53)
Neoadjuvant therapy, *n* (%)		29 (25)
Tumor characteristics		
Tumor size, cm; median (range)		5 (1.3–6.5)
T stage, *n* (%)		
	T0	0 (0)
	T1	2 (2)
	T2	3 (3)
	T3	112 (95)
	T4	1 (1)
N stage, *n* (%)		
	N0	36 (31)
	N1	82 (69)
Margin status, *n* (%)		
	R0	86 (73)
	R1	32 (27)
Status of splenic vein, *n* (%)		
	Ligated	87 (74)
	Reconstructed	31 (26)
Preserved critical vein, *n* (%)		
	SRCV arc	83 (70)
	MCV	10 (8)
	LGV	1 (1)
Spontaneous splenorenal shunt,* *n* (%)		
	Present	13 (11)
	Absent	105 (89)
Morbidity (Clavien-Dindo grade 3+), *n* (%)		18 (15)
	Mortality, *n* (%)	0 (0)

* A spontaneous splenorenal shunt was detected only in the follow-up imaging study.*SRCV arc*, superior right colic vein arcade; *MCV*, middle colic vein; *LGV*, left gastric vein.

the 3 critical veins, the SRCV arc was the most commonly persevered (70%), and the MCV and LGV were rarely preserved (8% and 1%, respectively). Although 35 patients (30%) had all 3 critical veins sacrificed, 10 patients (8%) had multiple critical veins preserved.

At 6 months after the operation, varices had developed in 44 patients (37% of the entire cohort), and when limited to the patients without a spontaneous splenorenal shunt, the incidence of development of SPH in patients who underwent PD with SpV ligation was 44% (33 among 75) if the SpV was not reconstructed. Among 44 patients who developed varices, 5 patients (4% of the entire cohort) developed GI bleeding from ruptured varices, occurring at a median of 17 months (7–23 months) postoperatively, and all were treated successfully with either open surgery or endoscopic or radiologic intervention. Table 2 presents a summary of the location of ruptured varices and the treatment administered for each patient. Of note, although 3 patients who underwent SpV reconstruction experienced GI bleeding from varices, none of their reconstructed SpVs were patent on CT at 6 months after the initial operation.

Preservation of critical veins reduced the risk of SPH after PD with SpV ligation

To elucidate perioperative factors associated with SPH after PD with SpV ligation, several preoperative and intraoperative variables were compared among the patients who developed varices and those who did not among the entire cohort. As presented in Table 3, absence of preserved critical veins was associated with increased risk of SPH (73% versus 4%, $P = < .001$) and presence of a spontaneous splenorenal shunt was associated with decreased risk of SPH (0% versus 18%, $P = .016$). Unexpectedly, intraoperative blood loss was less among the patients who developed varices than among those who did not (605 cc versus 800 cc, $P = .03$), and the relationship between blood loss and variceal formation was unclear. Because of the limited number of patients who underwent SpV reconstruction, we could not reliably evaluate the impact of SpV reconstruction on SPH in our analysis of the entire cohort.

Outcomes of splenic vein reconstruction and impact on SPH

SpV reconstruction can add complexity to an already complex PD with major vascular resection for advanced pancreatic cancer. Thus, we evaluated the outcomes for patients who underwent PD with SpV resection then undergoing splenic vein reconstruction compared with those for patients who underwent PD with SpV ligation alone. As summarized in Table 4, there were no significant differences in operation time, blood loss, and postoperative morbidity among the patients with and without SpV reconstruction. At the 6-month follow-up, the reconstructed vein remained patent only in 17 of the 31 patients (55%) who underwent SpV reconstruction. The incidence of SPH was not different among the patients who underwent SpV reconstruction and those who did not by intention-to-treat analysis (35.5% versus 37.9%, $P = .980$).

Risk stratification for SPH can select patients most likely to benefit from SpV reconstruction

A spontaneous splenorenal shunt is usually undetectable on preoperative imaging in patients without portal hypertension, thus we could not rely on this potential, "hidden" shunt to make a medical decision, and this patient group was excluded from the following analysis. To identify patients most likely to benefit from SpV reconstruction, we divided our remaining cohort into 3 groups based on the preserved critical veins and then analyzed the impact of successful SpV reconstruction on the incidence of SPH. As shown in Table 5, the number of preserved critical veins stratified the patients very well, according to the potential risk of SPH after PD with SpV ligation. Indeed, in patients in whom none of the 3 critical veins were preserved and no SpV reconstructions was performed after SpV ligation ($n = 29$), all (100%) developed SPH; in this same group with no critical veins preserved who had a successful SpV reconstruction ($n = 5$), SPH developed in 3 of the 5 patients. In patients with only 1 of the critical vein preserved and no

Table 2
Patients with ruptured GI varices after PD with SpV ligation.

Case number	Age (years)	Sex	Status of critical vein			SpVR	Status of SpVR	Interval from PD to event (month)	Site of bleeding	Treatment	Follow-up after PD (month)	Vital status
			SRCV arc	MCV	LGV							
1	68	F	–	–	–	No	NA	23	Pancreatojejunostomy	Splenectomy	57	DOD
2	38	F	–	–	–	No	NA	17	Gastrojejunostomy	Splenectomy	52	DOD
3	61	F	–	–	–	Yes	–	23/39	Hepatic flexure of colon	PSE/ Splenectomy	50	AWD
4	72	M	+	–	–	Yes	–	10	Pancreatojejunostomy	EVL	39	AWD
5	76	F	–	–	–	Yes	–	7	Hepatic flexure of colon	Splenectomy	18	AWD

SRCV arc, superior right colic vein arcade; *MCV*, middle colic vein; *LGV*, left gastric vein; *SpVR*, splenic vein reconstruction; +, patent; –, occluded; *NA*, not available; *PSE*, partial splenic embolization; *EVL*, endoscopic variceal ligation; *DOD*, dead of disease; *AWD*, alive with disease.

Table 3
Perioperative and intraoperative variables associated with SPH after PD with SpV ligation.

Variable	Patients with varices $n=44$	Patients w/out varices $n=74$	*P* value
Patient factors			
Age, years; median (range)	67 (37–86)	69 (42–84)	.27
Male sex, *n* (%)	27 (61)	36 (49)	.19
Presence of SSRS, *n* (%)	0 (0)	13 (18)	<.01
Neoadjuvant therapy, *n* (%)	10 (23)	19 (26)	.83
Operative factors			
Blood loss, mL; median (range)	605 (50–1900)	800 (110–2700)	.03
Operative time, min; median (range)	490 (363–920)	496 (431–989)	.17
Absence of preserved critical veins, *n* (%)	32 (73)	3 (4)	<.01
SpV reconstruction, *n* (%)	11 (25)	20 (27)	>.99
Postoperative factors			
Complications (G3+), *n* (%)	6 (14)	12 (16)	.80
Adjuvant chemotherapy, *n* (%)	41 (93)	66 (89)	.53

SSRS, spontaneous splenorenal shunt; *SpV*, splenic vein.

Table 4
Operative and long-term outcomes for SpV reconstruction.

	PD with SpVR n = 31	PD w/out SpVR n = 87	*P* value
Blood loss, mL; median (range)	590 (80–1830)	730 (50–2700)	.12
Operative time, min; median (range)	526 (393–727)	554 (363–989)	.51
# Critical vein preserved, *n* (%)			.68
0	11 (36%)	24 (28%)	
1	17 (55%)	56 (64%)	
> 1	3 (10%)	7 (8%)	
Complications (Grade 3+), *n* (%)	2 (7%)	16 (18%)	.15
Patent reconstructed SpV, *n* (%)	17 (55%)	NA	NA

PD, pancreatoduodenectomy; *SpVR*, splenic vein reconstruction; *SpV*, splenic vein; *NA*, not available.

Table 5
Impact of successful SpV reconstruction on SPH after SpV ligation according to the number of preserved critical veins ($n=105^{*}$).

Number of critical veins preserved	Incidence of SPH				*P* value
	SpVR open ($n=17$)		SpVR occluded or SpV ligated ($n=88$)		
0	3/5	(60%)	29/29	(100%)	.02
1	0/10	(0%)	12/51	(24%)	.19
≥ 2	0/2	(0%)	0/8	(0%)	NA

* Patients with SSRS were excluded.*SPH*, sinistral portal hypertension; *SpVR*, splenic vein reconstruction; *SpV*, splenic vein; *NA*, not available.

SpV reconstryuction, 12 of the 51 (24%) patients developed SPH; no SPH developed in a similar group of patients ($n=8$) with only 1 critical vein preserved when the SpV reconstruction was successful. In contrast, no patients with preservation of 2 or 3 of the critical veins ($n=8$) developed SPH, and thus there was no impact of SpV reconstruction on the outcomes for these patients.

Discussion

This cohort study of patients who underwent SpV ligation during PD with PV resection for pancreatic cancer demonstrated a high incidence of SPH; 37% of patients with SpV ligation developed varices in the gastrointestinal tract at 6 months postoperatively, and, of this group, 11% experienced life-threatening bleeding from their varices during follow-up. The preservation of critical veins appeared important in preventing SPH, with no patients who had at least 2 or all 3 of the critical veins preserved during PD developing varices. These observational findings highlight the clinical importance of this delayed complication after PD with complex vascular resection and the optimal use of SpV reconstruction for patients undergoing SpV resection/ligation for pancreatic cancer, according to the risk stratification.

Management of the SpV stump during PD with PV resection at the PMSC for patients with advanced pancreatic cancer has remained controversial throughout the past 2 decades, with recommendations both for and against SpV reconstruction not necessarily based on robust clinical evidence. For example, although some surgeons recommend SpV reconstruction when SpV-IMV confluence is not preserved, none have presented data on the incidence of SPH with SpV ligation nor the clinical implications of SpV reconstruction.[3-6,16]. In contrast, many opponents claim that SpV reconstruction is unnecessary simply because their patients never developed clinically relevant SPH in their small cohorts of 3 to 14 patients.[17–19] Indeed, little attention has been paid to SPH as a late consequence of PD with SpV ligation in studies reporting the outcomes for PD with PMSC resection,[20] and SPH is generally considered clinically unimportant for patients with advanced pancreatic cancer who have relatively short expected survivals. Nevertheless, in the modern era with improved operative safety for pancreatectomy and more effective chemotherapeutic regimens, patients with resectable pancreatic cancer requiring PV resection can live as long as those not needing PMSC resection.[21] Thus, the incidence of SPH after PD with SpV ligation needs to be reappraised, and reasonable criteria for SpV reconstruction should be established based on clinical evidence.

Among the limited data in the literature, the reported incidence of SPH or GI varices/splenomegaly ranges from 0% to 63%.[2,11,12] This apparently wide range in incidence of SPH among previous

studies can be explained by the heterogeneity in the preserved potential collateral veins draining into the portal system. Rosado et al[11] reported that only 25% of patients who underwent PD with SpV ligation developed nonruptured varices and concluded that SpV reconstruction is not necessary; however, although the IMV was routinely sacrificed, the majority of their patients had preservation of either the superior collateral routes (LGV or unnamed superior collateral veins [11/15]) or inferior collateral routes (MCV/SRCV arc or unnamed inferior collateral veins [14/15]). Similarly, Tanaka et al[2] reported a low incidence of SPH in 3 of 29 patients (10%) and also recommended against SpV reconstruction; however, when the patients were divided according to the preserved veins, 3 of the 6 patients (50%) without preservation of the LGV or IMV developed SPH, compared with 0 of 23 patients with preservation of LGV or IMV. In their series, the MCV was likely sacrificed in all patients, according to their previous work describing the technical details of their PD with PV resection,[22] although the status of SRCV arc was not documented in the report. In contrast, the majority of patients in the present cohort had their SRCV arc preserved, although the LGV and MCV were usually sacrificed, and the incidence of SPH was greater than in the 2 previous reports.

Based on earlier findings, we chose the LGV, MCV, and SRCV arc as critical veins in this analysis.[10–12] Some surgeons considered the IMV as one of the important collateral routes and recommended SpV-IMV anastomosis when SpV-IMV confluence cannot be preserved[3–6]; however, Strasberg's group reported a low incidence of varices in all of their patients with routine IMV division,[10,11] and furthermore, in our previous work, the incidence of varices was not different among patients with IMV preservation and those with the IMV sacrificed.[12] Thus, we maintain that the IMV does not have a great impact on the pathogenesis of SPH and thus, the IMV was not included among the critical veins. In addition, a spontaneous splenorenal shunt appears to become evident from an underlying congenital portosystemic shunt that is usually collapsed and undetectable by CT in patients with normal portal pressure, and it is reported most frequently in patients with liver cirrhosis with portal hypertension.[23–25] In our patient group, 11% showed the development of a spontaneous splenorenal shunt on CT after SpV ligation, and none of these individuals developed varices; because a spontaneous splenorenal shunt is implicated in the portal hemodynamics of patients after liver transplantation,[26] the impact of a "hidden" spontaneous splenorenal shunt on the development of SPH is likely to be crucial and important. Unfortunately, however, because of the difficulty in identifying a "hidden" spontaneous splenorenal shunt preoperatively or intraoperatively, we did not include it in our risk-stratification scheme for post-SpV-ligation SPH.

In terms of the optimal SpV reconstruction, there have been several recommendations, including splenorenal shunt using end-to-side anastomosis recommended by Katz et al[16] and Ferreira et al,[6] recommending SpV-IMV end-to-end anastomosis to restore SpV outflow after PD with PMSC resection; however, no outcomes data have been reported, and the long-term success in preventing SPH remains to be determined. In this study, we showed our early experience of SpV reconstruction, including when we first performed a spleno-gonadal shunt with end-to-end anastomosis, and, although our results showed that combined SpV reconstruction with PD did not increase operation time, blood loss, or postoperative complications compared with PD with SpV ligation alone, this observation needs to be interpreted with caution because of selection bias. Specifically, we did not necessarily attempt SpV reconstruction when the resection of the pancreatic tumor was technically difficult and thus would have taken a longer time or involved greater blood loss than usual. Nonetheless, SpV reconstruction is safe and technically feasible in experienced hands, and we remain in the middle of the learning curve with respect to reaching standardized reconstruction methods. Further refinements in operative techniques, reconstructive methods, and perioperative managements, such as the use of prophylactic anticoagulation therapy will be necessary to improve overall outcomes for SpV reconstruction.

Of particular note, this study revealed that the number of preserved critical veins could provide a useful guide for selecting patients most likely to benefit from SpV reconstruction. Such intraoperative consideration of the preservation of these critical veins makes sense intuitively in that patients with a greater number of preserved critical veins will have a lesser risk of developing SPH, and patients with all three critical veins sacrificed will most likely develop SPH and varices, and thus suggesting the need for a successful SpV reconstruction. In earlier work, we recommended preservation of the SRCV arc to prevent SPH[12]; however, the expanded cohort in this study suggested that preservation of only the SRCV arc is not sufficient as a preventive measure against SPH, because 16% of the patients with only 1 critical vein (the most with SRCV arc) developed GI varices. Thus, it seems that not only the number of veins but also the quality of veins (eg, caliber size, flow velocity) likely affect postoperative hemodynamics in the splenic outflow. Given that complete assessment of the hydrodynamics in each critical vein is not possible practically, we believe it is safe to consider SpV reconstruction unless when less than 2 of the critical veins are preserved during PD.

Despite the scale and novelty, our study has some limitations. First, the study design of retrospective review in a single institution incurs potential selection bias for patients; however, compared with other reports from high-volume centers, we had a much lower threshold for PV resection, and up to 63% of our PDs for pancreatic cancer were combined with PV resection. Furthermore, the PV branches, including the LGV and MCV, were commonly sacrificed to maximize PV mobility and to facilitate oncologic clearance. We also consider that the proposed risk-prediction scheme for classifying patients according to the number of preserved veins is theoretically applicable to all patients treated with different operative regimens. Second, our study focused on formation of GI varices as a sign of SPH, although patients with SPH can also present with splenomegaly and thrombocytopenia secondary to hypersplenism. Thus, we might underestimate the prevalence of SPH among our patients. We did not evaluate splenomegaly in this study because most patients were asymptomatic, and splenomegaly appeared clinically irrelevant for patients with pancreatic cancer. Finally, our outcome data for SpV reconstruction is possibly immature, attributable both to follow up as well as our developing experience with SpV reconstruction. And, with only 31 cases with nonstandardized various operative techniques, there remains much room for improvement regarding the optimal reconstructive technique for the strict evaluation of the success of SpV reconstructions. We do consider that our results in this study could serve as a proof-of-principle for the management of SpV stump after PD with PMSC resection, and further prospective evaluation for the outcomes for standardized SpV reconstruction will be necessary.

In summary, the incidence of GI varices after PD with PMSC resection for pancreatic cancer is not uncommon when SpV is simply ligated. The risk for varices is dependent on the number of critical veins preserved, and SpV reconstruction should be reserved for patients with less than two of the critical veins preserved. The careful preoperative assessment for critical veins and meticulous operative planning and techniques to preserve them are imperative to minimize the risk of SPH for patients with advanced pancreatic cancer.

Acknowledgments

The authors would like to thank Ms. Tomoko Shiode for her excellent support in manuscript preparation.

References

1. Hattori M, Fujii T, Yamada S, Inokawa Y, Suenaga M, Takami H, et al. Significance of the Splenic vein and its branches in pancreatoduodenectomy with resection of the portal vein system. *Dig Surg*. 2015;32:382–388.
2. Tanaka H, Nakao A, Oshima K, Iede K, Oshima Y, Kobayashi H, et al. Splenic vein reconstruction is unnecessary in pancreatoduodenectomy combined with resection of the superior mesenteric vein-portal vein confluence according to short-term outcomes. *HPB (Oxford)*. 2017;19:785–792.
3. Misuta K, Shimada H, Miura Y, Kunihiro O, Kubota T, Endo I, et al. The role of splenomesenteric vein anastomosis after division of the splenic vein in pancreatoduodenectomy. *J Gastrointest Surg*. 2005;9:245–253.
4. Christians KK, Riggle K, Keim R, Pappas S, Tsai S, Ritch P, et al. Distal splenorenal and temporary mesocaval shunting at the time of pancreatectomy for cancer: Initial experience from the Medical College of Wisconsin. *Surgery*. 2013;154:123–131.
5. Pilgrim CH, Tsai S, Tolat P, Patel P, Rilling W, Evans DB, et al. Optimal management of the splenic vein at the time of venous resection for pancreatic cancer: Importance of the inferior mesenteric vein. *J Gastrointest Surg*. 2014;18:917–921.
6. Ferreira N, Oussoultzoglou E, Fuchshuber P, Ntourakis D, Narita M, Rather M, et al. Splenic vein-inferior mesenteric vein anastomosis to lessen left-sided portal hypertension after pancreaticoduodenectomy with concomitant vascular resection. *Arch Surg*. 2011;146:1375–1381.
7. Loftus JP, Nagorney DM, Ilstrup D, Kunselman AR. Sinistral portal hypertension. Splenectomy or expectant management. *Ann Surg*. 1993;217:35–40.
8. Koklu S, Coban S, Yuksel O, Arhan M. Left-sided portal hypertension. *Dig Dis Sci*. 2007;52:1141–1149.
9. Liu Q, Song Y, Xu X, Jin Z, Duan W, Zhou N. Management of bleeding gastric varices in patients with sinistral portal hypertension. *Dig Dis Sci*. 2014;59:1625–1629.
10. Strasberg SM, Bhalla S, Sanchez LA, Linehan DC. Pattern of venous collateral development after splenic vein occlusion in an extended Whipple procedure: Comparison with collateral vein pattern in cases of sinistral portal hypertension. *J Gastrointest Surg*. 2011;15:2070–2079.
11. Rosado ID, Bhalla S, Sanchez LA, Fields RC, Hawkins WG, Strasberg SM. Pattern of venous collateral development after splenic vein occlusion in an extended Whipple procedure (Whipple at the splenic artery) and long-term results. *J Gastrointest Surg*. 2017;21:516–526.
12. Ono Y, Matsueda K, Koga R, Takahashi Y, Arita J, Takahashi M, et al. Sinistral portal hypertension after pancreaticoduodenectomy with splenic vein ligation. *Br J Surg*. 2015;102:219–228.
13. Takeda Y, Saiura A, Takahashi Y, Inoue Y, Ishizawa T, Mise Y, et al. Asymptomatic pancreatic cancer: Does incidental detection impact long-term outcomes? *J Gastrointest Surg*. 2017;21:1287–1295.
14. NCCN: National Comprehensive Cancer Network. NCCN guidelines version 2.2015 pancreatic adenocarcinoma Web site. https://www2.tri-kobe.org/nccn/guideline/archive/pancreas2015/english/pancreatic.pdf. Accessed April 1, 2018.
15. Inoue Y, Saiura A, Yoshioka R, Ono Y, Takahashi M, Arita J, et al. Pancreatoduodenectomy with systematic mesopancreas dissection using a supracolic anterior artery-first approach. *Ann Surg*. 2015;262:1092–1101.
16. Katz MH, Lee JE, Pisters PW, Skoracki R, Tamm E, Fleming JB. Retroperitoneal dissection in patients with borderline resectable pancreatic cancer: Operative principles and techniques. *J Am Coll Surg*. 2012;215:e11–e18.
17. Fujisaki S, Tomita R, Fukuzawa M. Utility of mobilization of the right colon and the root of the mesentery for avoiding vein grafting during reconstruction of the portal vein. *J Am Coll Surg*. 2001;193:576–578.
18. Launois B, Stasik C, Bardaxoglou E, Meunier B, Campion JP, Greco L, et al. Who benefits from portal vein resection during pancreaticoduodenectomy for pancreatic cancer? *World J Surg*. 1999;23:926–929.
19. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK, et al. Pancreaticoduodenectomy with en bloc portal vein resection for pancreatic carcinoma with suspected portal vein involvement. *World J Surg*. 2004;28:602–608.
20. Kim PT, Wei AC, Atenafu EG, Cavallucci D, Cleary SP, Moulton CA, et al. Planned versus unplanned portal vein resections during pancreaticoduodenectomy for adenocarcinoma. *Br J Surg*. 2013;100:1349–1356.
21. Zhou Y, Zhang Z, Liu Y, Li B, Xu D. Pancreatectomy combined with superior mesenteric vein-portal vein resection for pancreatic cancer: A meta-analysis. *World J Surg*. 2012;36:884–891.
22. Nakao A. The mesenteric approach in pancreatoduodenectomy. *Dig Surg*. 2016;33:308–313.
23. Uy PPD, Francisco DM, Trivedi A, O'Loughlin M, Wu GY. Vascular diseases of the spleen: A review. *J Clin Transl Hepatol*. 2017;5:152–164.
24. Achiwa S, Hirota S, Kako Y, Takaki H, Kobayashi K, Yamakado K. Radiological anatomy of spontaneous splenorenal shunts in patients with chronic liver disease. *Jpn J Radiol*. 2017;35:206–214.
25. Tarantino G, Citro V, Conca P, Riccio A, Tarantino M, Capone D, et al. What are the implications of the spontaneous spleno-renal shunts in liver cirrhosis? *BMC Gastroenterol*. 2009;9:89.
26. Golse N, Mohkam K, Rode A, Mezoughi S, Demian H, Ducerf C, et al. Surgical management of large spontaneous portosystemic splenorenal shunts during liver transplantation: Splenectomy or left renal vein ligation? *Transplant Proc*. 2015;47:1866–1876.