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Significance of the Splenic Vein and Its Branches in Pancreatoduodenectomy with Resection of the Portal Vein System

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Key Words
Pancreatoduodenectomy · Portal vein resection · Splenic vein · Inferior mesenteric vein · Sinistral portal hypertension

Abstract
Background/Aims: Pancreatic head carcinoma frequently invades the superior mesenteric vein (SMV) and/or portal vein (PV). We aimed to evaluate the outcome of transection of the splenic vein (SV) and inferior mesenteric vein (IMV) in pancreatoduodenectomy (PD) with SMV and/or PV resection. ***Methods:*** We retrospectively analyzed the records of 660 patients who had undergone pancreatectomy at our institution from January 2004 to October 2013, and selected 141 consecutive patients who had undergone PD with concurrent SMV/PV resection. Postoperative hypersplenism and the presence of remnant branches were evaluated. ***Results:*** The SV had been transected in 81 patients and preserved in 60. Postoperative complications and white blood cell counts were similar between the groups. The postoperative splenic volume was not significantly associated with the status of the SV or IMV on the transected SV. The platelet count was significantly lower, and the incidence of collateral veins was higher after SV transection than after SV preservation until 6 months after surgery; these variables were similar in the long term. ***Conclusion:*** SV reconstruction might be unnecessary when SV transection is required. Preservation of the IMV on the remnant SV might not prevent sinistral portal hypertension.

Introduction

Carcinoma of the pancreatic head frequently invades the superior mesenteric vein (SMV) and/or portal vein (PV) because of the close localization of these vessels with the pancreatic head. This invasion complicates the surgical procedure, even for small tumors of the pancreatic head. Vascular invasion was previously considered to be a contraindication for resection. However, patients with vascular invasion who undergo concurrent vascular resection sometimes achieve long-term survival equivalent to that in patients without vascular invasion [1–5]. In many specialized institutions, neoadjuvant chemoradiotherapy for locally advanced tumors is attempted to increase the rate of curative resection and improve survival [6–8].

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When resection involves the splenic vein (SV)/SMV confluence, the SV is almost always ligated and transected. Several investigators have reported that cessation of SV blood flow causes sinistral portal hypertension, which results in splenomegaly, gastric congestion, esophageal varices or thrombocytopenia [9]. Some authors have stated that SV ligation is safe and SV reconstruction is unnecessary in such cases, while others have raised concerns about adverse events such as sinistral portal hypertension after SV transection [10–18]. During SMV/PV/SV resection, surgeons sometimes hesitate in judging the validity of SV branch transection because there is no clear evidence for whether the branches should be preserved. The inferior mesenteric vein (IMV) drains directly into the SV in 51–68% of cases [14, 19, 20], and it is postulated that the preservation of the IMV can maintain the venous drainage of the spleen and gastric remnant, obviating the need for SV reconstruction. Some authors have emphasized the efficacy and necessity of additional anastomosis of the SV/IMV [14, 16]. However, the clinical significance of this anastomosis remains unclear because all such studies involved small cohorts (maximum of 39 cases) [16].

In the present study, the influence of SV transection during pancreatoduodenectomy (PD) with SMV and/or PV resection was evaluated. The effect of transection of the IMV was also investigated because this is thought to have the greatest influence on sinistral portal hypertension after SV ligation and transection.

Methods

Study Population

A prospectively maintained pancreatic resection database was queried to identify all cases of pancreatic head resection with SMV and/or PV resection. In total, 660 pancreatectomies were performed at the Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Japan, from January 2004 to October 2013. Of these 660 cases, 181 patients had undergone curative-intent pancreatectomy with SMV and/or PV resection for periampullary malignant neoplasms. Forty of these patients who had undergone total pancreatectomy, distal pancreatectomy or wedge resection of the SMV/PV were excluded because the principal purpose of the present study was to evaluate the significance of preservation of the SV and its branches in patients who had undergone PD. Consequently, 141 patients were enrolled.

Eighty-one (57.4%) patients had undergone SV/SMV confluence resection without SV reconstruction, 5 (3.5%) had undergone segmental circumferential PV resection and 55 (39.0%) had undergone segmental circumferential SMV resection. All patients had undergone end-to-end venous anastomosis, and none had undergone vascular graft placement or reconstruction of the transected SV. Written informed consent for retrospective analysis of various outcomes, as required by the Institutional Review Board of Nagoya University, was obtained from all patients.

Surgical Technique

Conventional PD with distal gastrectomy, subtotal stomach-preserving PD and pylorus-preserving PD have been previously described, and the surgical procedure performed was generally at the surgeon's discretion [21–23]. Although this study was retrospective in nature and only 3 or 4 surgeons performed the PD procedures, the surgical technique was almost identical among all of these surgeons. After intraperitoneal examination for metastasis, PD began via the mesenteric approach to achieve en bloc PD with a no-touch isolation technique [24, 25]. SMV and/or PV resection was performed in combination with standard pancreatectomy in cases of possible or definitive tumor invasion [26]. Whether to resect the SV/SMV confluence, PV or SMV was dependent upon the extent of tumor invasion. Vascular reconstruction was performed with a continuous 5-0 polypropylene suture in an end-to-end fashion. The SV branches were preserved, excluding those involved with the tumor.

Evaluated Factors

The blood count was compared between the SV preservation and transection groups preoperatively and at 1 and 21 days, 6 months, 1 and 2 years, postoperatively. The occurrence of postoperative sinistral portal hypertension and hypersplenism was also evaluated by assessing the splenic volume and the incidence of collateral vein appearance. The spleen area was measured by manual tracing of the spleen surface in 5-mm CT slices, and the volume was calculated by summation of the areas from all CT images. Esophageal and gastric collateral veins of grade ≥2 were defined according to the criteria reported by Kim et al. [27]. Briefly, grade ≥2 collaterals were diagnosed when esophageal, paraesophageal or gastric submucosal varices were >3 mm in their largest diameter or when gastric adventitial or retroperitoneal varices were >5 mm in their largest diameter. The appearance of collateral veins was evaluated on the CT images preoperatively and at 6 months, 1 and 2 years, postoperatively. The incidence of gastric or esophageal varices that had been confirmed endoscopically was also evaluated. Patients in the SV transection group were further categorized into 2 groups, whether these branches were preserved or transected. Subsequent data after cancer recurrence were excluded from the analysis.

Postoperative complications were evaluated according to the Clavien–Dindo classification [28, 29]. Pancreatic fistulae were estimated according to the classification system of the International Study Group on Pancreatic Fistula, and grade B or higher were considered to have clinical significance [30]. Delayed gastric emptying was defined according to the classification system of the International Study Group of Pancreatic Surgery, and grade B or higher were considered to have clinical significance [31].

Statistical Analysis

Differences in numerical data between the SV preservation and resection groups were examined using the χ^2 test or the Fisher's exact test when $n < 5$. Differences in quantitative variables between the 2 groups were evaluated using the Student's t test; the Mann–Whitney U test was used if the distribution was abnormal. The presence of a statistically significant difference was denoted by $p < 0.05$. All statistical analyses were performed using JMP software, version 10 (SAS Institute, Cary, N.C., USA).

Table 1. Demographic and clinical characteristics of the patients

	SV transection	SV preservation	p value
Patients, n	81	60	
Age, years, median (range)	65.0 (39–83)	66.0 (27–78)	0.905
Sex, male/female	44/37	33/27	0.964
Preoperative body mass index, median (range)	21.0 (13.6–33.3)	20.6 (15.1–32.1)	0.622
Preoperative diabetes	25	20	0.820
Preoperative biliary drainage	52	36	0.568
Disease			0.240
Pancreatic cancer	79	57	
Bile duct cancer	0	2	
Intraductal papillary mucinous carcinoma	1	0	
Endocrine neoplasms	0	1	
Metastatic tumor	1	0	
Operative method			0.089
Conventional PD	31	16	
Subtotal stomach-preserving PD	48	38	
Pylorus-preserving PD	2	6	
Operative time, min, median (range)	502 (342–960)	450 (220–685)	<0.001
Blood loss, ml, median (range)	1,242 (182–6,000)	794 (119–3,090)	0.002
Blood transfusion	24	11	0.107
Pancreatic texture, soft/hard	11/70	21/39	0.003
MPD diameter, mm, median (range)	5.0 (1–10)	4.0 (0.5–20)	0.080
Length of SMV/PV resection, mm			<0.001
Median (range)	30 (13–50)	20 (10–37)	
Mean ± SD	28.6±7.9	20.4±6.6	
Postoperative complications			
(Clavien–Dindo grade III or higher)	17	17	0.346
POPF (ISGPF grade B or higher)	11	7	0.701
DGE (ISGPS grade B or higher)	3	6	0.139
Mortality	0	0	1.000
Median length of hospital stay, days	33	33	0.813

MPD = Main pancreatic duct; POPF = postoperative pancreatic fistula; ISGPF = International Study Group on Pancreatic Fistula Definition; ISGPS = International Study Group of Pancreatic Surgery.

Results

Patient Characteristics and Perioperative Outcomes

The SV was transected in 81 patients and preserved in 60 (table 1). Age, sex and other preoperative characteristics were comparable between the SV transection and preservation groups. Primary diseases that were treated surgically were pancreatic cancer in all excluding 5 patients, bile duct cancer in 2 patients and an intraductal papillary mucinous carcinoma, endocrine neoplasm and metastatic tumor in 1 patient each. The median operative time was longer with SV transection than preservation (502 vs. 450 min, respectively; $p < 0.001$). The median blood loss was also significantly greater with SV transection than preservation (1,242 vs. 794 ml, respectively; $p = 0.002$). The median length of the resected vessel was significantly longer with SV transection than preservation (30 vs. 20 mm, respectively; $p < 0.001$). The overall postoperative complications, rate of postoperative pancreatic fistula formation, rate of delayed gastric emptying, and median length of hospital stay were equivalent between the 2 groups.

Comparison between the SV Transection and Preservation Groups

Postoperative outcomes were compared between the SV transection and preservation groups. To evaluate postoperative sinistral venous hypertension, the white blood cell count, hemoglobin level and platelet count were compared within 2 years after surgery. There were no differences between the 2 groups in the mean white blood cell count or hemoglobin level at 1 and 21 days, 6 months, 1 or 2 years, postoperatively (fig. 1a). The mean platelet count was significantly lower with SV transection than preservation at 21 days ($p = 0.009$) and 6 months

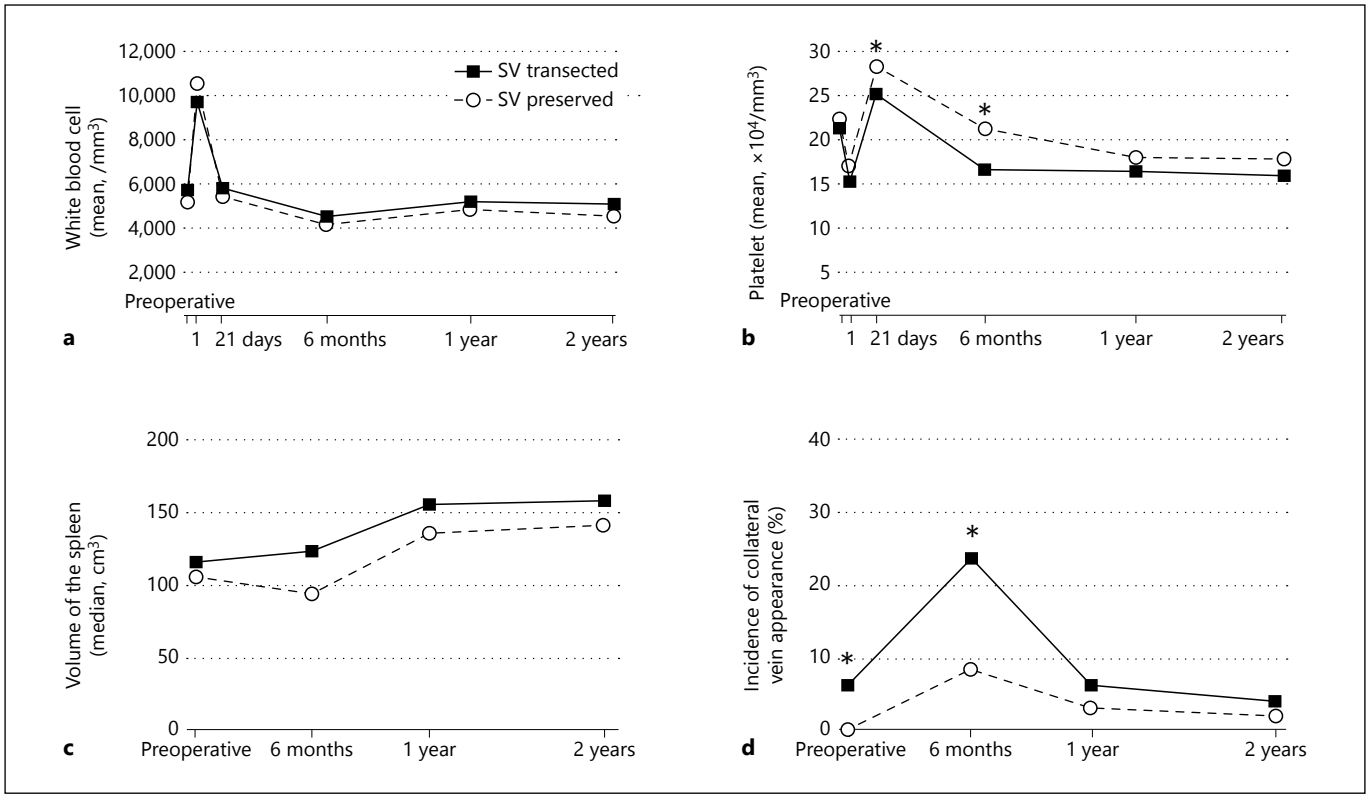

Fig. 1. Changes in white blood cell count (**a**), platelet count (**b**), splenic volume (**c**) and incidence of collateral veins (**d**). There was no significant difference in the white blood cell count between the SV transection and preservation groups. The platelet count was significantly lower with SV transection than preservation at 21 days and 6 months, postoperatively, but equivalent at 1 and 2 years after surgery between the 2 groups. The postoperative splenic volume tended to be greater in the SV transection group, although the difference did not reach statistical significance. The incidence of collateral veins was significantly higher with SV transection than preservation at 6 months after surgery; however, there were no significant differences at 1 and 2 years, postoperatively, between the 2 groups. * Significant difference between the 2 groups.

postoperatively (p = 0.016), but was equivalent at 1 and 2 years postoperatively between the 2 groups (fig. 1b). The splenic volume tended to be higher with SV transection than preservation, although the difference did not reach statistical significance at 6 months, 1 and 2 years after surgery (fig. 1c). The incidence of collateral veins was significantly higher in the SV transection group preoperatively and at 6 months, postoperatively; however, there were no significant differences at 1 and 2 years postoperatively between the 2 groups (fig. 1d).

Influence of Remnant Branches of SV on Hypersplenism

To evaluate the hemodynamics after SV transection, the patients were further categorized into 2 groups according to the presence of the IMV on the transected SV (fig. 2). Postoperative hypersplenism was compared among the following 3 groups according to the above-

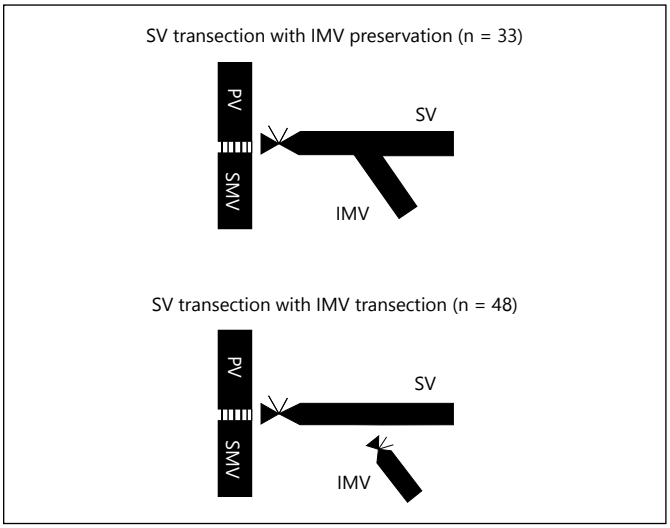

Fig. 2. Classification according to the presence of the IMV after SV transection.

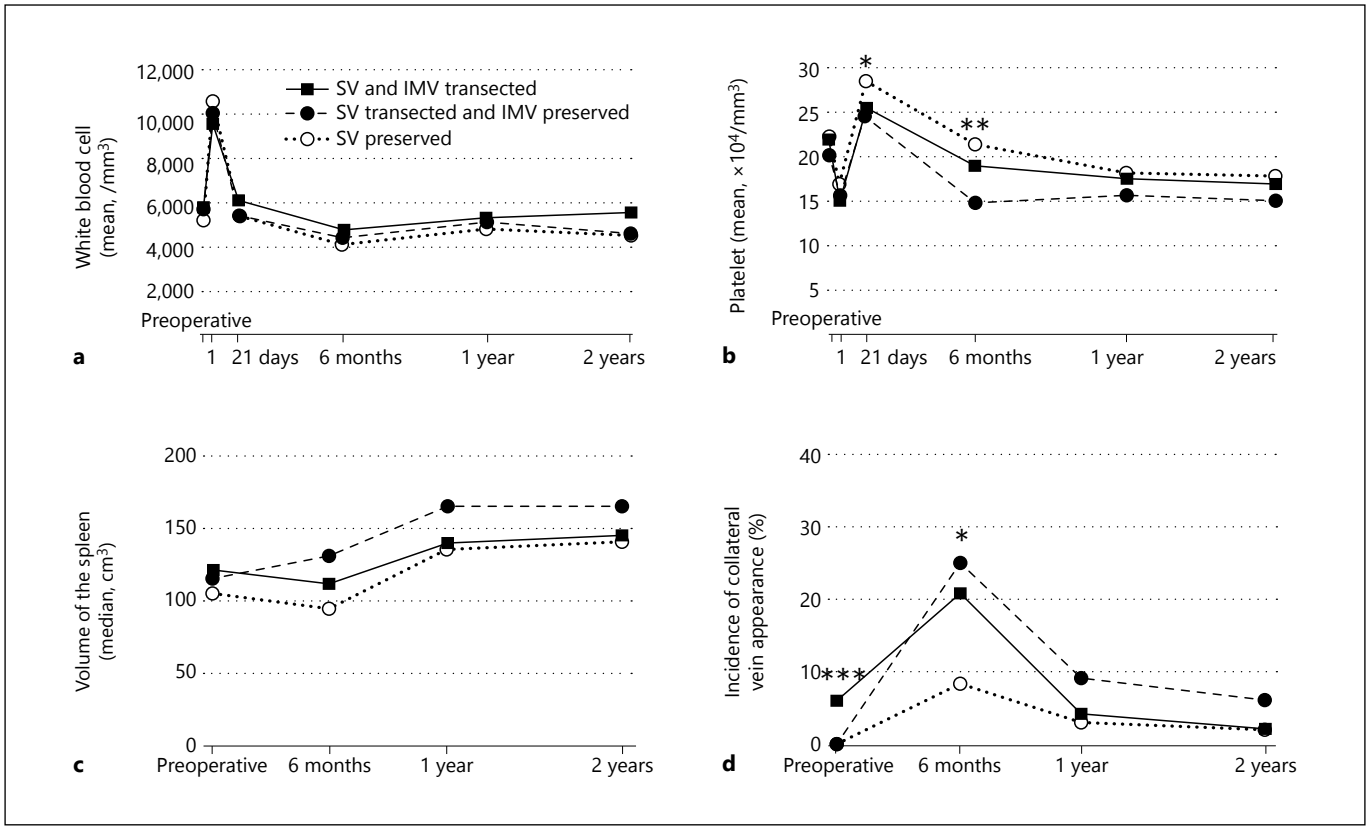

Fig. 3. Influence of the presence of the IMV on hypersplenism in SV transection. **a** There were no significant differences in the white blood cell count among the 3 groups. **b** The platelet count at 6 months, postoperatively, was significantly lower in the SV transection with IMV preservation group than in the SV preservation group, although the differences were not statistically significant at 1 and 2 years, postoperatively. **c** The splenic volume was increased in the SV transection group; however, no significant difference was found postoperatively among the 3 groups. **d** The incidence of collateral vein appearance was almost equivalent at 1 and 2 years, postoperatively, among the 3 groups. * Significant difference between the SV preservation group and the other 2 groups. ** Significant difference between the SV preservation group and the SV transection with IMV preservation group. *** Significant difference between the SV preservation group and the SV transection with IMV transection group.

described classification to evaluate the influence of the IMV on the transected SV: SV transection with IMV preservation (n = 33), SV transection with IMV transection (n = 48) and SV preservation (n = 60). There were no significant differences in the white blood cell count among the 3 groups after surgery (fig. 3a). The platelet count at 6 months postoperatively was significantly lower in the SV transection with IMV preservation group than in the SV preservation group (p = 0.003), although the difference was not statistically significant at 1 and 2 years, postoperatively (fig. 3b). The splenic volume increased in the SV transection group; however, no significant difference was found postoperatively among the 3 groups (fig. 3c). There were no significant differences in the incidence of collateral veins at 1 and 2 years, postoperatively, among the 3 groups (fig. 3d).

Endoscopic evaluation was performed in 23 patients of the SV preservation group, and in 31 patients of the SV transection group. Gastric or esophageal varices that were endoscopically confirmed as symptoms of postoperative sinistral portal hypertension were found in 3 patients (13.0%) in the SV preservation group and in 7 patients (22.6%) in the SV transection group (p = 0.372). Treatment for variceal rupture was required in 1 patient in each group.

Discussion

We analyzed 141 patients who underwent SMV and/or PV resection and compared the postoperative outcomes between the patients with and without SV transec-

tion. The postoperative splenic volume tended to be greater in the SV transection group, although no significant difference was found between the 2 groups. The mean platelet count was significantly lower in the SV transection group until 6 months postoperatively. Our study confirmed the generally accepted hypothesis that SV transection can lead to sinistral portal hypertension, which results in splenomegaly and thrombocytopenia. However, the platelet count, although lower after SV transection, did not reach statistical significance at 1 and 2 years after surgery. Thus, we suggest that SV reconstruction is not always necessary after PV/SMV resection from the long-term perspective.

Patients in the SV transection group were categorized depending on the presence of the IMV. No significant differences were found in the postoperative splenic volume among all the groups. The splenic volume tended to be higher with preservation of an IMV that flowed into the remnant SV. The platelet count was lower in patients in the SV transection with IMV preservation group. Some authors have described the importance of preservation of the SV/IMV confluence or SV/IMV anastomosis, and surgeons usually consider preserving the major branches, especially the IMV, when the SV requires transection. However, our results seem to contradict the concept that preservation of an IMV that flows into the remnant SV can avoid sinistral portal hypertension [14, 16, 32, 33]. Although the blood in the remnant SV is believed to flow in an anterograde direction through the anastomosis or confluence into the IMV, the flow might proceed in the opposite direction in some patients, resulting in enhanced sinistral portal hypertension over the long term. One hypothesis is that interruption of SV flow leads to the formation of another collateral vein besides the IMV, followed by a change in the direction of IMV flow over the longer term, thus increasing SV flow. However, Misuta et al. [14] reported that retrograde blood flow from the IMV into the remnant SV is revealed on postoperative venography in some patients, leading to splenomegaly and venous dilation around the stomach. Therefore, efforts to preserve the IMV or perform SV/IMV anastomosis are not invariably beneficial. To the best of our knowledge, no other study has conducted a similar analysis in a patient cohort of this size.

One limitation of our study is that it was a retrospective analysis; however, it might be difficult to design a prospective controlled trial. Moreover, the long-term morphological and hematological changes after SV transection were demonstrated in this study; however, the long-term hemodynamic changes should be explored by venography or ultrasonography to clarify the mechanisms involved in these changes.

Conclusion

SV reconstruction might be unnecessary when SV transection is required. Preservation of an IMV that drains into the remnant SV does not necessarily prevent sinistral portal hypertension.

Disclosure Statement

No financial or other potential conflicts of interest exist for any of the authors.

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