



Clinical Impact of Intraoperative Navigation Using a Doppler Ultrasonographic Guided Vessel Tracking Technique for Pancreaticoduodenectomy

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During pancreaticoduodenectomy (PD), early ligation of critical vessels such as the inferior pancreaticoduodenal artery (IPDA) has been reported to reduce blood loss. Color Doppler flow imaging has become the useful diagnostic methods for the delineation of the anatomy. In this study, we assessed the utility of the intraoperative Doppler ultrasonography (Dop-US) guided vessel detection and tracking technique (Dop-Navi) for identifying critical arteries in order to reduce operative bleeding. Ninety patients who received PD for periampullary or pancreatic disease were enrolled. After 14 patients were excluded because of combined resection of portal vein or other organs, the remaining were assigned to 1 of 2 groups: patients for whom Dop-Navi was used (n = 37) and those for whom Dop-Navi was not used (n = 39; controls). We compared the ability of Dop-Navi to identify critical vessels to that of preoperative multi-detector computed tomography (MD-CT), using MD-CT data, as well as compared the perioperative status and postoperative outcome between the 2 patient groups. Intraoperative Dop-US was

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significantly superior to MD-CT in terms of identifying number of vessels and the ability to discriminate the IPDA from the superior mesenteric artery (SMA) based on blood flow velocity. The Dop-Navi patients had shorter operation times (531 min versus 577 min; no significance) and smaller bleeding volumes (1120 mL versus 1590 mL; $P < 0.01$) than the control patients without increasing postoperative complications. Intraoperative Dop-Navi method allows surgeons to clearly identify the IPDA during PD and to avoid injuries to major arteries.

Key words: Pancreaticoduodenectomy – Doppler ultrasonography – Blood flowmeter

Pancreaticoduodenectomy (PD) is a standard treatment for malignant tumor of periampullary and pancreas head. As lymphatics (lymph node and lymph vessels) accompany the arteries and are distributed in the surrounding neural plexuses, complete clearance of peripancreatic tissue, including lymphatics and nerve plexus, is necessary for curative resection of the tumor.^{1–4} As this operation is considered a complex procedure, a surgeon is required to be well trained in this specific surgical technique and to possess sufficient anatomic knowledge.

Despite a low mortality rate and improvements in perioperative care and operative management, there is still a relatively high complication rate following PD.^{5,6} Several studies showed that intraoperative bleeding and red blood cell (RBC) transfusion are serious risk factors of postoperative complications in PD.^{6,7} Recently, several procedures for artery-first approaches such as posterior, uncinated, and mesenteric approach have been introduced for improving perioperative outcomes such as curability and decreasing blood loss and morbidity.^{8–11} Incidentally, it has been well known that early ligation of the inferior pancreaticoduodenal artery (IPDA)—one of the efferent arteries of the pancreas head—considerably reduces intraoperative bleeding and postoperative complications.^{12–14} Owing to the various anatomic origins of IPDA, identification is difficult in some patients. Therefore, some groups have attempted to locate the origin of IPDA by preoperative enhanced multi-detector computed tomography (MD-CT) and 3-dimensional angiogram using MDCT data (3D-CT angiography).^{12,13} In addition, an augmented reality technique using MD-CT data is being considered an innovative navigation system for PD.¹⁵ However, no simple intraoperative guidance system, which would greatly facilitate the complex procedure of vessel ligation and reduce intraoperative bleeding, has been tested for ligation of the IPDA during PD.

Intraoperative ultrasonography provides useful information for diagnosis and for guidance during the hepatobiliary-pancreatic surgery.^{16,17} Color Doppler flow imaging facilitates to delineate the anatomy and to identify the vascular structures invading malignant tumors.^{18–22} Recently, advanced navigation techniques have been introduced, such as 3D-CT angiography and intraoperative ultrasonography.^{21–24} Doppler ultrasonography (Dop-US) has been used as an effective method for detecting the presence of potential bleeders.^{25,26} However, Dop-US-assisted intraoperative identification and tracking of critical vessels for pancreatic surgery has not been reported to date.

The objective of the present study was to evaluate the potential of intraoperative Dop-US for detection of critical vessels relative to that of preoperative MD-CT, including MPR and 3D angiography, and to clarify the efficacy of vessel navigation surgery using Dop-US-guided tracking for the reduction of intraoperative bleeding.

Methods

Patients

Ninety patients who underwent PD for benign or malignant disease of the periampullary and pancreatic region at the Kagoshima University Hospital between January 2007 and August 2012 were selected. From these, 14 patients who underwent portal vein resection ($n = 10$) or combined resection other organs, including hilar bile duct ($n = 4$), were excluded in order to standardize the operative method as much as possible. Finally, 76 patients were included in the study. Forty-seven patients were men, and the average age was 65.7 years (range, 30–85 years); all patients were Japanese. This study was approved by the Human Studies Group at the Kagoshima University School of Medicine. All patients gave their written informed consent before participation.

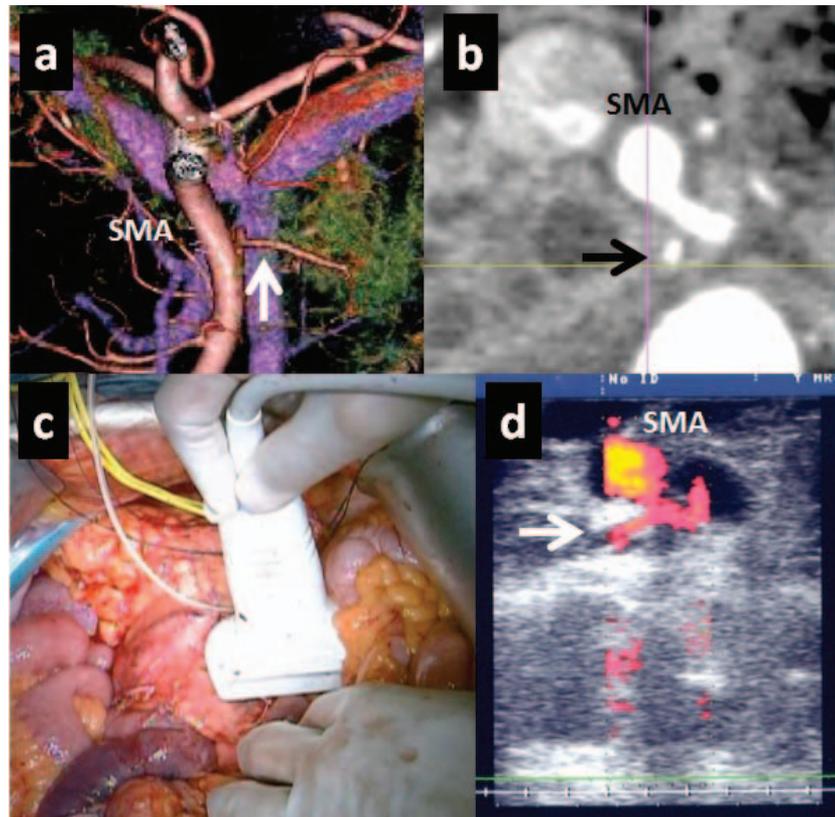


Fig. 1 Intraoperative Doppler ultrasonography. (a) A rear view of a volume-rendered image showing arteries (red), the portal system (purple), the pancreatic parenchyma (green), and the inferior pancreaticoduodenal artery (IPDA; black arrow). (b) Multiplanar reconstruction image of the bifurcation of IPDA (black arrow). (c) Intraoperative examination around the pancreas head. (d) Doppler ultrasonogram of the IPDA diverging from superior mesenteric artery (SMA) using power Doppler mode (white arrow).

Surgical procedures

The patients underwent pylorus-preserving pancreaticoduodenectomy (PPPD) or subtotal stomach-preserving pancreaticoduodenectomy (SSPPD). The surgery involved D1 or D2 lymphadenectomy, according to the classification of the Japan Pancreas Society's sixth edition of General Rules for the Study of Pancreatic Cancer.²⁷ D1 lymphadenectomy only involved the removal of the lymph nodes around the pancreatic head, whereas D2 lymphadenectomy was defined as resection of the area along the hepatoduodenal ligament, the common hepatic artery, the superior mesenteric artery, and the peripyloric tissue. The pancreatic neural plexus comprises 2 branches: PLX-I, which originates from the right celiac ganglion and runs behind the portal vein to enter the pancreas between the uncinate process and the abdominal nerve ganglion, and PLX-II, which originates in the superior mesenteric artery (SMA) plexus and extends into the uncinate process along the pancreaticoduodenal artery and the jejunum trunk.

After the surgical procedure, treatment success was evaluated in terms of residual tumor (R) categories defined as follows: R0, no residual tumor;

R1, microscopic residual tumor; and R2, macroscopic residual tumor.

Preoperative evaluation of the peripancreatic head vessels by MD-CT

A 16-detector-row MD-CT scanner (Aquilion; Toshiba Medical Systems, Tochigi, Japan) was used to obtain CT images. The scan delays from the administration of contrast material to the start of arterial, pancreatic parenchymal, and portal venous phases were fixed at 25, 43, and 70 seconds, respectively. Since 2005, 3D-CT angiography has been performed for preoperative evaluation of critical vessels around the SMA, such as the IPDA. The images were reformatted with 1-mm-thick multiplanar reconstruction (MPR) and 3D-CT angiograms and volume-rendered images of the pancreatic parenchyma on a workstation (Exavision; Ziosoft, Inc, Tokyo, Japan). The locations of the arteries were preoperatively analyzed using MPR and 3D imaging (Fig. 1a and 1b).

Intraoperative vessel navigation using Dop-US

Intraoperative Dop-US was performed using the power Doppler mode with the ultrasonography

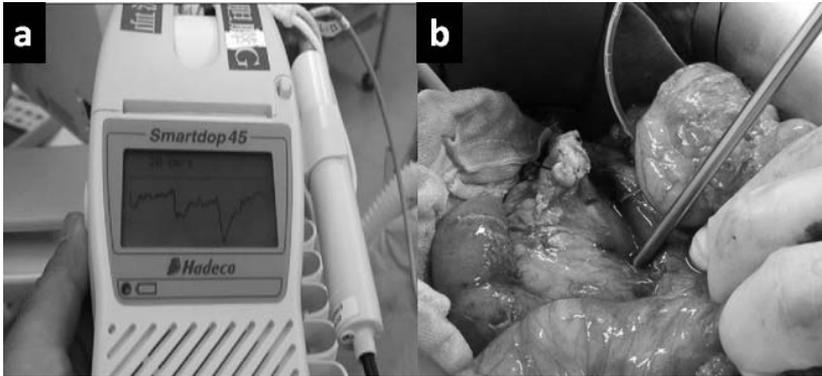


Fig. 2 Intraoperative vessel detection and tracking of an artery around the pancreas head using Doppler blood flowmeter. (a) Displayed waveform of vessel blood flow in the device LCD, (b) Real time tracking of the artery using a thin, rod-shaped ultrasonography probe.

probe connected to a high-end ultrasound scanner (Pro Sound SSD-5500; Hitachi Aloka Medical, Ltd, Tokyo, Japan) before resection of the neural plexuses of the pancreas head and those surrounding the SMA (Fig. 1c and 1d). First, we scanned the pancreas head along the SMA. Then, we identified all bifurcations of the pancreaticoduodenojunal (PDJ) trunk and the IPDA and other branches. Next, early ligation of IPDA method was performed using intraoperative vessel navigation by Dop-US guidance (Dop-Navi). The procedures of this technique were as follows: (1) the operator identified the SMA and the PDJ trunk or the IPDA visualized by Dop-US; (2) real-time detection and tracking of the SMA and IPDA around the pancreas were performed with a bidirectional Dop-US blood flowmeter (ES-100V3; Hadeco, Kawasaki, Japan; Fig. 2a) and a thin probe (LRP08; Hadeco, Kawasaki, Japan; Fig. 2b); (3) the detected IPDA was exposed and ligated at the root of the bifurcation to

reduce bleeding from the pancreatic parenchyma during the dissection of the connective tissue and nerve plexuses around the SMA. The blood flow data from the SMA and IPDA acquired with the Dop-US blood flowmeter were recorded for analysis (Fig. 3a and 3b).

Statistical analysis

The 76 patients were assigned to 1 of 2 groups by chronologic order: the first 39 patients were evaluated by preoperative MD-CT and 3D-CT angiography only (the control group), and the subsequent 37 patients were evaluated by preoperative MD-CT and 3D-CT angiography followed by Dop-Navi (the Dop-Navi group). Intraoperative Dop-US images were compared to preoperative images from MPR and 3D-CT angiograms created from the MD-CT data. The mean number of arteries and artery diameters except SMA obtained by Dop-US, MPR, or 3D-CT angiogram were compared by 1-way analysis of variance (ANOVA), followed by a Tukey post-hoc test. The maximum and mean blood flow velocities of the SMA and IPDA acquired from the Dop-US flowmeter were compared using Student's *t*-test, or the nonparametric equivalent, the Mann-Whitney *U* test. The following perioperative data were collected: texture of pancreas evaluated by intraoperative palpation; type of resection; lymph node dissection level; SMA plexus dissection; residual tumor classification; operation time; bleeding volume; red blood cell transfusion. Delayed gastric emptying was defined by the International Study Group of Pancreatic Surgery.²⁸ Pancreatic fistula was defined by the International Group of Pancreatic Fistula.²⁹ Perioperative factors and postoperative complications in the 2 groups were compared using a chi-squared test. All data are expressed as the mean \pm

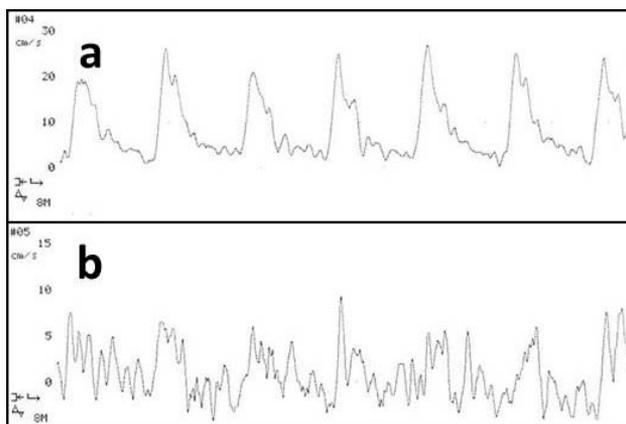


Fig. 3 Waveforms of the SMA (a) and IPDA (b) recorded by Doppler blood flowmeter. Wave shape and velocity are quite different in both.

Table 1 Characteristics of the enrolled patients

	Control	Dop-Navi	P-value
Mean age ± SD, years	65.1 ± 9.9	67.8 ± 8.7	0.2248
Male/Female	23/16	24/13	0.5972
Mean body mass index ± SD	23.1 ± 3.4	21.9 ± 2.3	0.0993
Diabetes mellitus, n	9	4	0.1558
Biliary drainage, n	11	13	0.6771
Primary lesion			
Pancreas, n	24	20	
PDAC, n	9	8	
IPMN, n	11	8	
Other, n	4	4	
Bile duct, n	7	13	
Vater, n	6	3	
Duodenum, n	2	1	
Final pathology			
Benign/Malignant	8/31	4/33	0.2974

Dop-Navi, Dop-US-guided vessel tracking navigation group; SD, standard deviation; IPMN, intraductal papillary mucinous neoplasm; PDAC, pancreatic ductal adenocarcinoma.

standard deviation (SD). Statistical significance was defined as $P < 0.05$.

Results

Patient characteristics

Comparisons of clinical preoperative parameters and the histological results of the control and Dop-Navi groups are shown in Table 1. As all patients had a tumor that was diagnosed as malignant or low malignant preoperatively, lymph node dissection

was performed for all of them. However, the tumors of 12 patients were diagnosed as benign in final pathologic analysis. There was no statistically significant difference between the 2 groups with respect to body mass index, diabetes mellitus, preoperative biliary drainage, or histologic type.

Assessment of intraoperative Dop-US-guided vessel detection

The information obtained intraoperatively about the pancreatic vessels by Dop-US was compared to the preoperative MD-CT scans analyzed by MPR and 3D angiography (Fig. 4a and 4b). First, there was a significant difference in the number of vessels detected by the 3 imaging modalities (ANOVA, $P < 0.05$). Dop-US (Tukey test; $P < 0.0001$), and MPR (Tukey test; $P = 0.0022$) detected significantly more vessels in the pancreatic head than 3D angiography (Fig. 4a). In addition, these techniques also differed in terms of mean diameter (ANOVA, $P < 0.01$), with significantly lower values obtained with Dop-US (Tukey test; $P < 0.0001$) and MPR (Tukey test; $P = 0.0069$), indicating higher definition (Fig. 4b). These data are consistent with the higher success rate of Dop-US and MPR in the identification of the IPDA within the pancreatic tissue. These data show that intraoperative Dop-US is as efficient as preoperative 3D-CT scans analyzed by MPR for visualizing of critical vessels around the SMA.

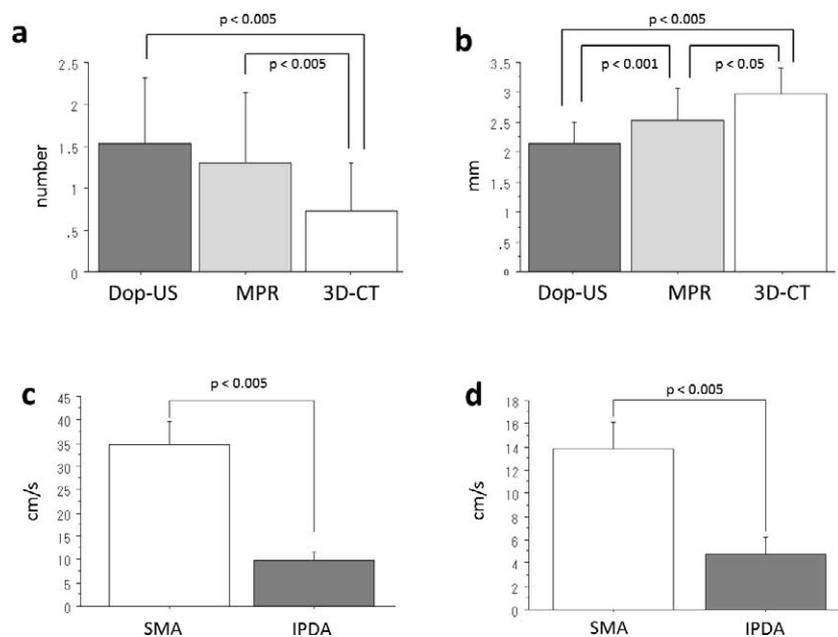


Fig. 4 (a) Comparison of detected number of arteries in the pancreatic tissue around the SMA. (b) Comparison of the minimum diameter of detected arteries except SMA. (c, d) A comparison of blood flow velocity between the SMA and IPDA. The intraoperative blood flow velocity of IPDA measured using a blood flowmeter was significantly lower than that of the SMA for both maximum (c) and mean (d) velocity.

Table 2 Perioperative status and postoperative complications in Dop-Navi surgical patients and control patients

	Control	Dop-Navi	P-value
Perioperative status			
Pancreatic texture (Hard/Soft)	12/27	9/28	0.6508
Type of resection (PPPD/SSPPD)	10/29	7/30	0.4776
Lymph node dissection level (D1/D2)	22/17	14/23	0.0822
SMA plexus dissection, n	8	8	0.9520
Residual tumor classification (R0/R1)	34/5	36/1	0.0885
Mean operation time \pm SD, min	577 \pm 113	531 \pm 109	0.0723
Mean bleeding volume \pm SD, mL	1590 \pm 866	1120 \pm 629	0.0093
Mean RBC transfusion \pm SD, mL	334 \pm 501	168 \pm 358	0.1057
Postoperative complications			
Abscess (intraabdominal, liver), n	6	0	
Biliary leakage, n	1	1	
DGE, grade B or C, n	2	1	
Intraabdominal hemorrhage, n	0	1	
Pancreatic fistula, grade B or C, n	1	1	
Total, n	8	5	0.4180

SD, standard deviation; SMA, superior mesenteric artery; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; R0, no residual tumor; R1, microscopic residual tumor; RBC, red blood cell; DGE, delayed gastric emptying.

Assessment of intraoperative Dop-US-guided vessel tracking

During surgery, identification of the IPDA is complicated by the surrounding nerve plexus tissue in the proximity of the SMA. Intraoperative real-time Dop-US revealed that the 2 vessels exhibit distinct bloodstream waveforms (Fig. 3a and 3b). As the IPDA had a markedly smaller waveform than the SMA, the flowmeter was able to trace the IPDA, which flowed into the parenchyma of the pancreatic head during the operation. The maximum blood flow velocity in IPDA was 3 times lower than that in the SMA ($P < 0.005$; Fig. 4c). In addition, the mean blood flow velocity in the IPDA was 2.5 times lower than that in the SMA ($P < 0.005$; Fig. 4d). These data demonstrate the ability of intraoperative real-time Dop-US to identify and track the vessels targeted for ligation during the PD procedure.

We also compared the perioperative data of the 2 groups (Table 2). The 2 groups were subjected to the same surgical procedures, in terms of PPPD/SSPPD, lymph node dissection level, and SMA plexus dissection frequencies. Only 2% (1/36) of the patient monitored using Dop-Navi method had residual tumor (R1) tissue after surgery, compared to 14% (5/34) in the control group patients who were only assessed by preoperative CT. The R1 site was the surgical edge of the bile duct in the hepatic side or the distal main pancreatic duct (data not shown). The operation time and volumes of RBC transfusions were less in the Dop-Navi group, but there were no significant differences. In contrast, the Dop-

Navi group had a significantly reduced bleeding volume (1120 mL versus 1590 mL; $P < 0.01$).

No severe postoperative complications or deaths were observed in either group. There were no significant differences in the frequency or type of postoperative complications (Table 2). A Grade B pancreatic fistula occurred in 2 patients, both of whom recovered with conservative treatment.

Discussion

Complete resection of pancreatic head tumors by PD is a very complex surgical procedure involving the ligation of numerous vessels. The imaging techniques used by surgeons to navigate this network of vessels and nerves are limited to preoperative 3D-CT, which do not accommodate tissue displacement during the operation. While IPDA ligation reduces intraoperative bleeding, the root of the IPDA is not always identified on preoperative 3D-CT.^{12,13} The present study demonstrates the potential of intraoperative critical vessel detection by Dop-US and the efficacy of real-time vessel navigation by Dop-US-guided tracking technique to facilitate IPDA identification and early ligation, while reducing intraoperative bleeding.

Recently, Dop-US has been successfully used to obtain detailed blood flow images for various organs and organ systems such as the cardiovascular system, kidney, hepatobiliary-pancreatic system, and spleen.^{18,30} The Dop-US appearances of peri-pancreatic vessels have been well documented and

are well visualized even if the examination is performed through the abdominal wall.²² As we were able to place the ultrasound probe on the surface of the pancreatic parenchyma directly during the operation, the acquired view of pancreatic tissue around the SMA was quite clear. Each artery detected by intraoperative Dop-US completely correlated with the MPR imaging and 3D-CT angiogram. Moreover, our method could also visualize small arteries with diameters of less than 2 mm. It was difficult to recognize these small arteries on 3D-CT angiogram. By using Dop-US, we were able to clearly visualize the PDJ trunk and the bifurcation of the IPDA in most patients without exposing the patient to ionizing radiation or contrast media. We determined that intraoperative Dop-US, in the power Doppler mode, was better than MD-CT for precise visualization of vessels.

It is well known that the IPDA usually branches on the dorsal side of the SMA and runs along the inside of the pancreatic nerve plexus tissue anatomically. It was not easy to use the conventional method to locate the IPDA in the operative field when the operation was performed with an anterior approach, despite having acquired preoperative imaging. The Doppler blood flowmeter can measure blood velocity during the operation.²² Ultrasonography-guided operations are performed in the fields of neurosurgery and urology.^{26,31} Usually, it is not easy to recognize the arteries that run into the pancreatic nerve plexus around the SMA intraoperatively without palpation. A thin, rod-shaped probe enabled real-time detection of the precise location of the arteries, which were located in the neural plexus of the pancreas head. As our results show, the waveform and flow velocity data acquired using the Doppler blood flowmeter were quite different between the IPDA and SMA, which enabled the surgeon to quickly and easily recognize the location of both arteries.

To perform safe and effective resection of cancer of the pancreas head, it is very important to identify the vascular ramification patterns around the pancreas head in each patient. Kawai *et al*¹³ reported that early ligation of the IPDA using preoperative CT imaging before isolation of the pancreas head was useful for reducing intraoperative bleeding in PD. Horiguchi *et al*¹² showed that locating the IPDA preoperatively and intraoperatively with MD-CT imaging is a similarly effective approach to safely perform PD. However, MD-CT images acquired preoperatively cannot be easily transposed on the real-time view of the operative

field. On the other hand, ultrasonography is a very useful and non-invasive technique that provides real-time information during dissection. As our procedures controlled the critical vessels such as IPDA and/or PDJ trunk prior to complete dissection of the connective tissue between pancreas and SMA safely, we considered that insidious bleeding from dissected pancreatic tissue was avoided during the operation. As PD consists of many complicated procedures, we tried to evaluate our technique simply by elimination of the patients who underwent additional invasive procedures such as portal vein resection or combined resection of other organs. However, the patients who enrolled in this study were not randomized in the Dop-Navi group or control group. In addition, it was not sufficient to elucidate the predominance of our technique because of the primary lesion diversity and the sample size. Unfortunately, it seems difficult to clarify the effect of this procedure, because this study did not take an accurate measurement of bleeding volume in each procedure particularly. It is necessary to demonstrate how the Dop-Navi method contributes to achieving a reduction of intraoperative bleeding volume by a prospective study.

It is well known that a strong advantage of ultrasonographic examination is noninvasiveness. Nevertheless, intraoperative Dop-US has been used only for the diagnosis of tumor spread or assessment of blood flow volume in the pancreas to date.^{32,33} The Dop-Navi procedure is also a very simple method where the surgeon or surgical assistant only needs to put the probe on the pancreas tissue to directly hear the Doppler sound during the operation. Inflammation due to biliary drainage sometime causes chronic tissue change, which interferes with continuing the operation around bile duct. As there was no significant difference of biliary drainage rate between both groups, it was also thought to be equal to the influence of inflammation from tumor in both groups. The Dop-Navi group had shortened total operation time in spite of additional procedures. This examination did not contribute to an increase in the length of the procedure or increase operative complications. We demonstrated that this vessel navigation strategy is quite easy and useful for avoiding injury of critical arteries in the pancreatic field and for reducing operative bleeding volume without requiring palpation. Therefore, this technique might be utilized by less

experienced surgeons or in advanced laparoscopic surgery.

In conclusion, the present study demonstrates that intraoperative navigation using Dop-US guided vessel detection and real-time tracking technique allows surgeons to clearly identify the IPDA during PD while avoiding injuries to major arteries. This simple and easy imaging technique contributes to improving the overall efficiency of pancreatic surgery by reducing bleeding volume without extension of the operative time.

Acknowledgments

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