

ORIGINAL ARTICLE

No-Touch Total Mesopancreas Excision for Pancreatic Head Cancer

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ABSTRACT

Pancreatectomy, specifically R0-resection, is the only effective treatment for pancreatic head cancers. The frequent recurrence of cancers within the resection bed may be due to inadequate removal of the so-called mesopancreas margin. Furthermore, surgeons usually grasp tumors during pancreatectomy. However, this practice may increase the risk of cancer cell shedding. In an effort to overcome these problems, we have ameliorated our no-touch pancreatoduodenectomy technique for total mesopancreas excision. The approach allows the tumor to be resected without grasping, and is intended to enable total resection of the mesopancreas. In the current series, 71% of the pancreatoduodenectomy performed for pancreatic ductal adenocarcinoma was R0 resections. Overall and recurrence-free 5-year survival rates after surgery were 42 and 32%, respectively. Those rates of 36 patients after R0 resection were 56 and 39%, respectively. No-touch total mesopancreas excision improved the surgical outcomes except morbidity. This technique may have many theoretic advantages, which merit further investigation in future randomized controlled trials.

INTRODUCTION

R0-resection is the only effective treatment for pancreatic cancers. The frequent recurrence of cancers locally, within the resection bed, may be due to inadequate clearance of the peripancreatic retroperitoneal margin, the so-called mesopancreas [1, 2, 3, 4]. In fact, after careful study of surgical specimens, some recent reports emphasized that few patients actually undergo true R0-resection. Attempts to reduce the frequency of recurrence have resulted in numerous modifications to existing pancreatoduodenectomy (PD) techniques [5, 6, 7, 8, 9]. It is possible that complete mesopancreas clearance might be achieved with an extended PD; however, this procedure can potentially lead to intractable diarrhea. Furthermore, since piecemeal resection is more likely to lead to cancer cell spillage than *en bloc* resection, the potential benefits of extending the dissection planes are compromised. In an effort to overcome these problems, we have developed a surgical technique known as total mesopancreas excision (TMPE) for improved dissection of the mesopancreas.

The term mesopancreas was introduced recently, with an analogical reference to the terms, mesorectum and total mesorectal excision for rectal cancer. The mesopancreas is also known as the (peripancreatic) retroperitoneal margin. The mesopancreas represents the neurovascular bundle, which includes the pIph-I, pIph-II, inferior pancreatoduodenal artery, 1st jejunal artery and vein, and lymph nodes [8, 9]. Because pancreatic cancer invasion is characterized not only by lymphatic involvement but also by perineural invasion, simple nodal excision has been traditionally considered to be oncologically inadequate. Consequently, skeletonization of the regional vessels with removal of the lymph nodes in addition to the perivascular neural and soft tissues is recommended. From this perspective, it should be noted that skeletonization should be performed on the right side of the superior mesenteric artery (SMA) and the celiac artery (CA) at their origins [8, 9].

The no-touch isolation technique was originally adopted as a strategy to protect cancer cells from shedding during colon and eye cancer surgery [10, 11]. Because pancreatic tumors are traditionally grasped by the surgeon prior to the ligation of surrounding vessels, the shedding-risk of cancer cells into the portal vein, retroperitoneum, and/or peritoneal cavity can be increased during pancreatectomy [12, 13]. Hence, there is a potential benefit in using a no-touch approach during pancreatectomy [13, 14, 15]. In an effort to overcome these problems and to further improve the efficacy of TMPE, we devised a surgical technique for improved *en bloc* mesopancreas dissection without grasping tumors, namely "no-touch TMPE" (Figure 1).

Received April 06th, 2017-**Accepted** April 29th, 2017
Keywords Pancreatoduodenectomy; Pancreatic Neoplasms; Pancreas
Abbreviations PD pancreatoduodenectomy; TMPE total mesopancreas excision
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SURGICAL TECHNIQUE

Dissection of the Portal Venous System

After transection of the gastric antrum, hilar bile duct, pancreatic neck, and proximal jejunum, all portal vein tributaries are ligated and divided individually. If the tumor is suspected to or has invaded the superior mesenteric and portal veins (SMV/PV), the affected SMV/PV is resected. The affected SMV/PV is later reconstructed. If necessary, the reconstruction is performed with the help of an antithrombogenic catheter bypass [16].

Pre-aortic Tunneling and Cord-taping

The peritoneum and the connective tissue adjacent to the abdominal aorta are next dissected between the ligament of Treitz and the inferior mesenteric vein. The anterior surface (adventitia) of the abdominal aorta, which corresponds to the posterior plane of the Gerota fascia, is exposed. To permit the passage of a cord, blunt dissection of the anterior surface of the aortic adventitia is performed in a cranial direction along the right side of the SMA and CA (Figures 2a,b). This plane can be easily dissected if there is no cancer invasion or inflammatory adhesion. Upon lifting the cord, the plane posterior to the Gerota fascia and anterior to the aorta can be further dissected bluntly.

Hanging Up and Clamping of the Mesopancreas

Cranial end of the cord is repositioned to the pancreatic side of the common hepatic artery and PV, and caudal end to the pancreatic side of the left renal vein and mesocolon (Figure 2c). At this point, the cord lifts up the mesopancreas (retroperitoneal margin adjacent to the

SMA), including the CA and SMA neural plexuses, lymphatic vessels, and the inferior pancreaticoduodenal artery, by hanging it up (hanging maneuver). The pancreatic side of the mesopancreas is held using a long-nosed, right-angled DeBakey type aortic clamp (Figure 2d). The DeBakey type aortic clamp is suitable for clamping the mesopancreas, because it fits the shape of the resecting mesopancreas margin.

Transection of the Mesopancreas

With the support of rightward traction of the clamp, the mesopancreas is transected along the right surface of the SMA and abdominal aorta. A step-by-step scooping of the tissue along the SMA allows identification of the inferior pancreaticoduodenal artery, as well as the replaced right hepatic artery (in case). The other side of the dissected tissue is ligated to inhibit lymphatic leakage (Figure 3). It should be emphasized that the tumor never serves as a "handle for retraction" of the specimen.

Reversed Kocher's Maneuver

The last procedure of the resection includes reversed Kocherization. The posterior plane of the Gerota fascia is dissected inside-to-outside, allowing exposure of the left renal vein and inferior vena cava until the *en-bloc* PD is completed. The mesopancreas margin is sliced along the right-angled clamp and is subjected to frozen microscopy. After the completion of *en bloc* PD, extensive peritoneal lavage was performed with 10 L of warm saline to remove any potential dissemination of cancer cells in all enrolled patients. Reconstruction is performed according to the surgeon's preference.

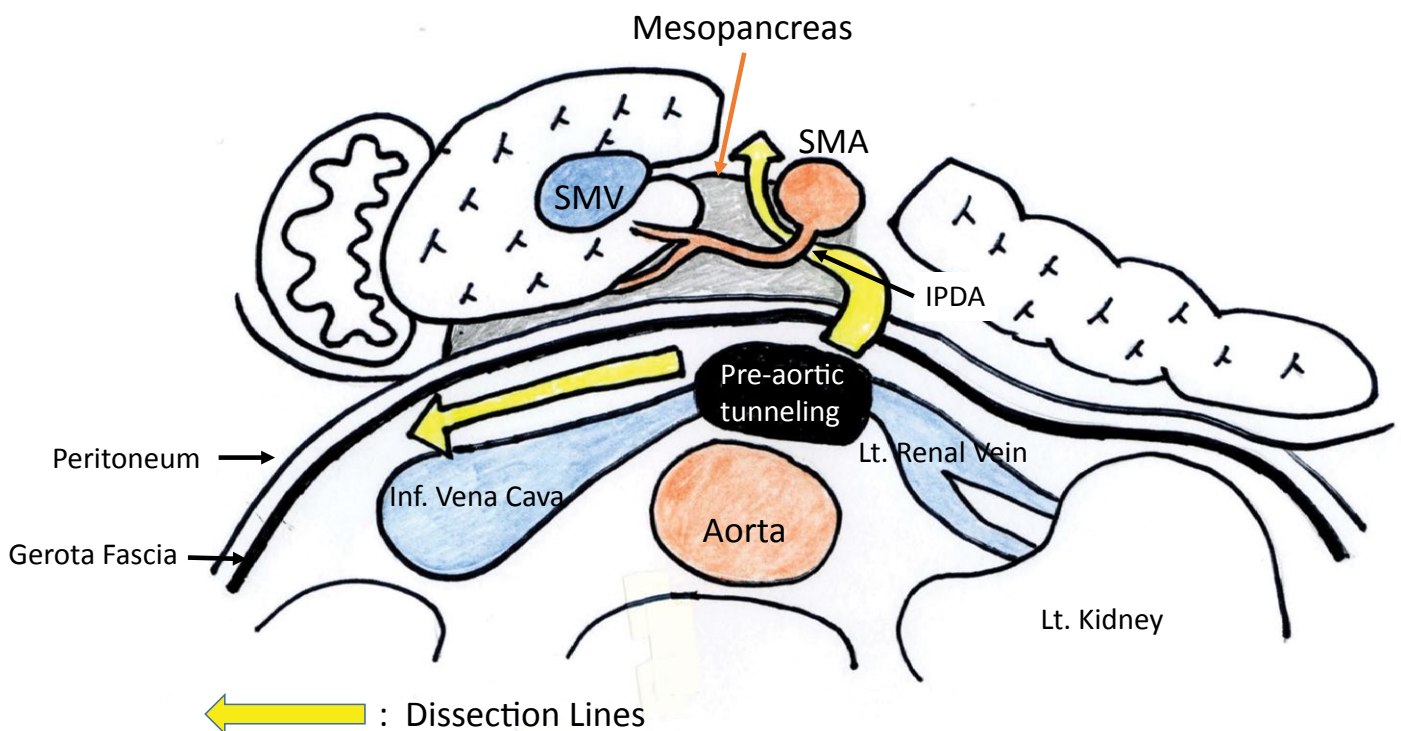


Figure 1. Schematic depiction of the mesopancreas and the dissection lines in no-touch TMPE.

The anterior surface of the abdominal aorta, which corresponds to the posterior plane of the Gerota fascia, is exposed and is dissected further horizontally. This plane is easy to dissect if there is neither cancer invasion nor inflammatory adhesion. The mesopancreas margin is then transected vertically along the right surface of SMA the and CA.

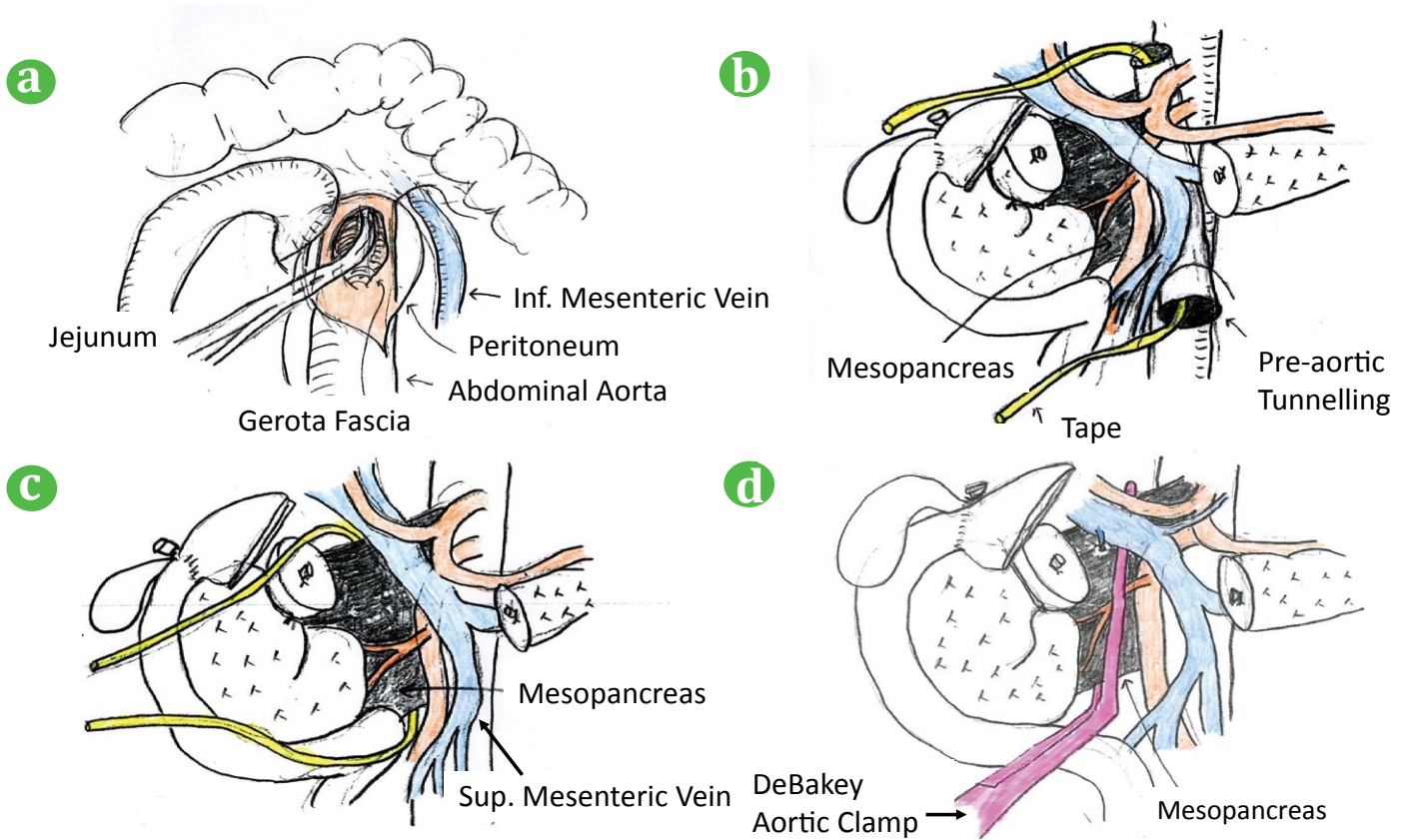


Figure 2. Hanging up and clamping of the mesopancreas.

(ab). The anterior surface of the aorta is dissected bluntly to permit the passage of a cord. After repositioning the cord, (cd), the pancreatic side of the mesopancreas is clamped using a right-angled DeBakey type aortic clamp.

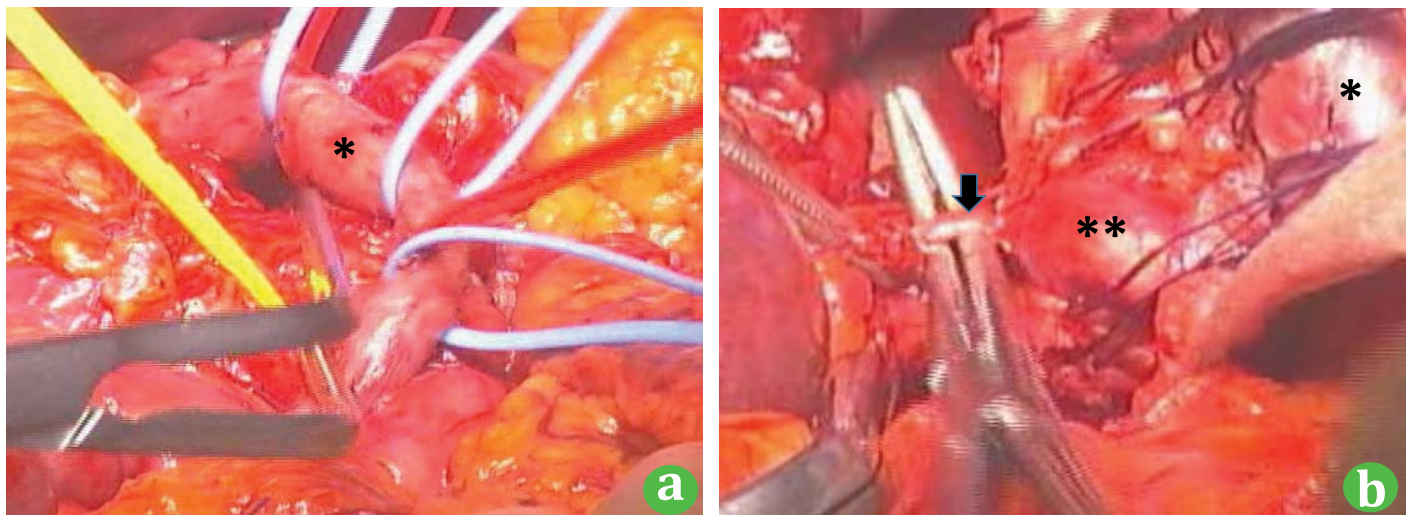


Figure 3. Clamping and division of the mesopancreas.

After clamping of the mesopancreas, (a), the mesopancreas margin is transected along with the right surface of the SMA (**). (b). A step-by-step scooping of the tissue along the SMA allows identification of the inferior pancreaticoduodenal artery (arrow) *: SMV/PV.

RESULTS

From April 2008 through December 2016, 51 patients with pancreatic ductal adenocarcinoma have been operated upon using this technique with written informed consents. Of the patients with pancreatic ductal adenocarcinoma, 25 cases (49%) required SMV-PV resection. As for the tumor stages in these patients, the final pathological stage classification according to the Japan Pancreas Society was I/II/III/IVa/IVb for 1/0/25/16/9 patients. The International Union against Cancer stage according to the

pathological tumor-node-metastasis classification was IA/IB/IIA/IIB/III/IV for 1/0/20/27/1/2 patients.

Among these cases, there was 0% hospital mortality. Postoperative complications were as follows: 3 patients with Grade B/C pancreatic fistula (6%), 3 with anastomotic ulcer (6%), 2 with liver abscess (4%), 2 with pneumonia (4%), 1 with necrosis of the transverse colon (2%), 1 with bleeding from the right hepatic artery (2%), 1 with infection of the central venous catheter (2%), and 1 with sepsis (2%). Overall morbidity rate was 27%.

Resected margins were microscopically analyzed. Intraoperatively, bile duct cut-end margins, pancreatic cut-end margins and mesopancreas margins (peripancreatic retroperitoneal margins) were confirmed to be free of tumor using frozen microscopy. Among the cases, 36 (71%) were R0, 12 (24%) were R1, and 3 (6%) were R2. Overall and recurrence-free 5-year survival rates of all 51 patients after surgery were 42 and 32%, respectively. Those rates of 36 patients after R0 resection were 56 and 39%, respectively. In one patient (76 years of age at surgery), the microscopic positive mesopancreas margin was negative after additional resection of the tissue around the SMA. The patient survived 7.5 years after the surgery and died due to renal failure without tumor recurrence.

DISCUSSION

We described here a PD technique involving a hanging up/clamping maneuver for TMPE. Because this approach permits tumor resection without any grasping or squeezing, the technique has been named "no-touch TMPE".

The no-touch TMPE technique allows for proper clearance of the tissue along the SMA, CA and abdominal aorta. This maneuver is used to facilitate negative resection margins. Many studies confirmed the importance of R0 resection for pancreatic head cancers [4, 17, 18, 19]. Rightward traction of the clamp on the mesopancreas is supposed to improve the clearance of the nervous and lymphatic tissues along the SMA and CA. The traction procedure may increase the possibility achieving R0 resection of pancreatic ductal adenocarcinoma.

Another important benefit of the technique is the potential reduction in the shedding of cancer cells. Pancreatic tumors are traditionally grasped by surgeons before the ligation of surrounding vessels during pancreatectomy. Grasping of the tumor prior to ligation of the involved vessels may increase the risk of cancer cell shedding. We previously reported the presence of cancer cells in droplets (exudate) from resected pancreatic tissues containing cancer lesions [13]. Similarly, Ishikawa reported the presence of potentially viable cancer cells in the postoperative drainage fluid from the pancreatic bed [19]. The drain cytology is a more specific predictor of subsequent local recurrence [19]. For no-touch TMPE, all drainage veins from the pancreas are ligated and divided during the early phase of the surgery, and during the procedure, the pancreatic tissues containing cancer lesions are not grasped by the surgeons.

In severe acute pancreatitis, autodigestion of the peripancreatic fat tissue (fat necrosis) is generally initiated. Whereas the perirenal fat tissue beyond the Gerota fascia is often protected from autodigestion [20]. The Gerota fascia may function as a barrier for autodigestion by pancreatic protease. Because cancer invasion is also dependent on protease activity of the cancer cells, the Gerota fascia can also be a barrier for cancer invasion. One of our aims was to resect cancers by wrapping the tissues with the Gerota

fascia. Whether this component of the resection procedure proves to be of clinical importance will be a topic of future investigations.

Our overall and recurrence-free survival rates were better than in standard PD. No-touch TMPE procedure using the hanging and clamping maneuver for mesopancreas resection improved the surgical outcomes except morbidity. This technique may have many theoretic advantages, which merit further investigation in future randomized controlled trials.

Acknowledgments

The authors thankfully appreciate Ms. Kazumi Isechi for support of the clinical data management of the pancreatic cancer patients.

Conflict of Interest

The authors have declared that no competing interests exist.

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