# Treatment of Advanced Pancreatic Body and Tail Cancer by En Bloc Distal Pancreatectomy with Transverse Mesocolon Resection Using a Mesenteric Approach

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**Background:** Pancreatic body and tail cancer easily invades retroperitoneal tissue, including the transverse mesocolon. It is difficult to ensure a dissected peripancreatic margin with standard distal pancreatectomy for advanced pancreatic body and tail cancer. Thus, we developed a novel surgical procedure to ensure dissection of the peripancreatic margin. This involved performing dissection deeper than the fusion fascia of Toldt and further extensive en bloc resection of the root of the transverse mesocolon. We performed distal pancreatectomy with transverse mesocolon resection (DP-TCR) using a mesenteric approach and achieved good outcomes.

**Methods:** There are two main considerations for surgical procedures using a mesenteric approach: 1) dissection deeper than the fusion fascia of Toldt (securing the vertical margin) and 2) modular resection of the pancreatic body and tail, with the root of the transverse mesocolon and adjacent organs in a horizontal direction (ensuring the caudal margin).

**Results:** From 2017 to 2019, we performed DP-TCR using a mesenteric approach for six patients with advanced pancreatic body and tail cancer. Histopathological radical surgery was possible in all patients who underwent DP-TCR. No Clavien-Dindo grade IIIa or worse perioperative complications were observed in any patient.

**Conclusions:** We believe that DP-TCR is useful as a radical surgery for advanced pancreatic body and tail cancer with extrapancreatic invasion. (J Nippon Med Sch 2021; 88: 301–310)

Key words: distal pancreatectomy, mesenteric approach, pancreatic body and tail cancer

# Introduction

Pancreatic body and tail cancer easily invades retroperitoneal tissue, including the transverse mesocolon, and is a major factor that hinders the curability of surgery<sup>1-5</sup>. In standard distal pancreatectomy (anterior approach)<sup>6-9</sup> for cancer invasion deeper than the fusion fascia of Toldt (generic term, including Gerota fascia) and for cancer invasion progressing toward the root of the transverse mesocolon, the principal problem is the difficulty in ensuring that the dissected peripancreatic margin (DPM) and posterior peripancreatic margin (PPM)<sup>10,11</sup> are cancernegative. In addition, en bloc resection of micro-lymph node metastasis and local dissemination is difficult. Therefore, we developed a novel surgical procedure to ensure dissection of the peripancreatic margin: we used the mesenteric approach performed in isolated pancreatoduodenectomy for advanced pancreatic head cancer, which was first described by Nakao<sup>12-14</sup>. This involved dissection and cleaning deeper than the fusion fascia of Toldt and further extensive en bloc resection of the root

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Fig. 1 a: Cephalocaudal section of the upper abdomen. The root of the transverse mesocolon transitions into the retroperitoneal tissue without serous membrane. The fusion fascia of Toldt is located in the retroperitoneal tissue. For extrapancreatic cancer invasion, the fusion fascia of Toldt serves, to some extent, as a barrier on the dorsal side of the pancreas.

b: In distal pancreatectomy with transverse mesocolon resection, the region resected en bloc is shown in color as a module.



Fig. 2 In the mesenteric approach, the middle colic artery and accessory right colic arteries are clamped with bulldog forceps to test colonic blood flow. Arrowheads: marginal vessels of the transverse colon

of the transverse mesocolon. Furthermore, we performed distal pancreatectomy with transverse mesocolon resection (DP-TCR) using a mesenteric approach and achieved good outcomes.

## Patients and Methods

The present procedure is indicated for advanced pancreatic body and tail cancer invading the retroperitoneal tissue, including the transverse mesocolon, without distal metastasis other than controlled peritoneal dissemination within the omental bursa (stage I-IV; presence of dissemination in the omental bursa only)<sup>10,15</sup> (**Fig. 1a and b**). Furthermore, with regard to invasion of the superior mesenteric artery (SMA), surgery is indicated for patients for whom resection is deemed possible by dissection of the SMA nerve plexus. Concurrent distal pancreatectomy with celiac axis resection is possible in some patients<sup>4,16,17</sup>. Moreover, while efforts are made to preserve the marginal vessel of the transverse colon and maintain blood flow of the transverse colon (**Fig. 2**), if blood flow in the transverse colon is poor after completing excision, concurrent resection of the transverse colon can be performed without hesitation. We decided to use DP-TCR preoperatively, not during surgery, when CT indicated that cancer cells had invaded extrapancreatic tissues. By contrast, we used standard DP preoperatively or during surgery when we determined that cancer cells remained within pancreatic parenchyma.

There are two main considerations for this surgical procedure. First, for extrapancreatic cancer invasion, the procedure aims to secure the vertical and horizontal margins. Dissection by the mesenteric approach is appropriate for securing both margins.

# Dissection Deeper than the Fusion Fascia of Toldt with the Mesenteric Approach: Securing the Vertical Margin

After elevating the transverse colon to the cranial side, dissection is initiated from the root of the transverse mesocolon. A mesenteric approach is used to dissect the root of the transverse colon (**Fig. 3a**) and circumferentially dissect the superior mesenteric vein (SMV) and SMA on the ventral side of the horizontal portion of the duodenum. The surgeon then proceeds to dissect toward the root of the SMA and ligate and section the middle

#### DP Using Mesenteric Approach



Fig. 3 a: The serosa of the transverse mesocolon is sectioned from the third portion of the duodenum to the terminus of the ligament of Treitz (origin of jejunum), thereby commencing the mesenteric approach.

\*Ligament of Treitz

- b: The dorsal side of the fusion fascia of Toldt is directly accessed using the mesenteric approach.
- \*Ligament of Treitz
- c: After sectioning the left adrenal vein, the anterior to the abdominal aorta and dorsal to the left adrenal gland are dissected.

colic artery (MCA), to reach the celiac nerve plexus. The goal of dissection around the root of the MCA is not merely lymph node dissection but to ensure an adequate surgical margin for advanced pancreatic body and tail cancer.

Subsequently, the surgeon proceeds to dissect as much as possible toward the left crus of the diaphragm from the left celiac nerve plexus, and to simultaneously resect the ligament of Treitz that continues on the left side of the SMA nerve plexus from the abdominal aorta toward the celiac nerve plexus from the origin of the jejunum. The nerves, lymph nodes, and adipose tissue around the SMA dorsal to the fusion fascia of Toldt and surrounded by the ventral side of the SMA and ventral side of the ligament of Treitz are dissected, cleaned, and attached to the fusion fascia of Toldt (resected side) (Fig. 3b). Furthermore, the anterior surface of the abdominal aorta is dissected dorsal to the ligament of Treitz, and the nerves, lymph nodes, and adipose tissue surrounding the dorsal side of the ligament of Treitz and the ventral side of the abdominal aorta are cleaned. During surgery, proceed with circumferential dissection of the left renal vein, ligation and dissection of the left adrenal vein, and dissection of the left adrenal gland. Thereafter, lift the left adrenal gland dorsally, thus enabling combined resection without dividing the ventral surface of the left adrenal gland and the fusion fascia of Toldt (**Fig. 3c**). This manipulation is extremely important in ensuring the most dorsal vertical margin.

Modular Resection of the Pancreatic Body and Tail with Adjacent Organs in a Horizontal Direction Using the Mesenteric Approach: Ensuring the Caudal Margin

When considering extrapancreatic cancer invasion of the pancreatic body and tail in a horizontal direction, examination can be divided into the coronal direction and cephalocaudal direction (from head to tail). With regard to coronal direction, the left side extends to the spleen and poses no clinical problem; on the right side, there is no resection limit, unless total pancreatectomy is a consideration. However, if total pancreatectomy is contraindicated, the point up to the line connecting the gastroduodenal artery and intrapancreatic bile duct can be considered. With regard to the cephalocaudal direction (from head to tail), the common hepatic artery, celiac axis, and splenic artery (SA) form a protective wall on the cranial side. However, the caudal direction poses a problem. Cancer invading dorsally outside the pancreas continues to invade retroperitoneal tissue, where there are no large protective organs up to the transverse colon. To ensure a cancer-negative margin in such circumstances, en bloc resection of the root of the transverse mesocolon on the left side of the SMV, together with the pancreas body and tail as the module, is the only suitable method.

In the anterior lobe of the transverse mesocolon, retroperitoneal tissue, and posterior lobe of the transverse mesocolon (in the bare area), en bloc dissection is completed by the layer reaching the ventral side of the left renal vein via the ventral side of the ligament of Treitz from the tissue on the ventral side of the SMA nerve plexus. In this situation, it is important that the dissected tissue be dissected en bloc with the body and tail of the pancreas as the module.

In the layer where the prepancreatic head-duodenal fascia is resected with the third portion of the duodenum as the starting point, the omental bursa is released from the cranial side of the pancreas. Skeletonization of the SMV and portal vein (PV) is performed and, with regard to branches flowing in from the left side of the main trunk of the SMV, only the inferior mesenteric vein and inferior pancreatoduodenal vein are preserved, as indicated by preoperative CT. The splenic vein is ligated and dissected; however, the left of the inferior border of the pancreas and transverse mesocolon (all layers) are not separated (Fig. 4a). The area from the common hepatic artery to the SA should be cleaned to the greatest extent possible, to determine the cranial margin of the resected specimen. The SA is then ligated and dissected, and upon cutting the pancreas at the anterior surface of the PV, the fusion fascia of Toldt remains, while the ventral and dorsal sides are completely dissected (Fig. 4b). After dissecting the fusion fascia of Toldt at the left margin of the PV, the anterior surface of the SMA nerve plexus, which has been dissected to ensure the vertical margin, is exposed. As a result, the pancreas forming the right margin of the resected specimen, the anterior lobe of the transverse mesocolon, the retroperitoneal tissue more superficial than the fusion fascia of Toldt, the fusion fascia of Toldt, and the retroperitoneal tissue deeper than the fusion fascia of Toldt are all resected en bloc (Fig. 4c). The subsequent procedures are identical to those used for radical antegrade modular pancreatosplenectomy (RAMPS)18, namely, dissection proceeds toward the left subphrenic space on the dorsal side along the crus of the

diaphragm.

Dissection on the left side of the origin of the jejunum is performed after elevating the transverse colon to the cranial side. To allow effective visualization of the surgical site of the retroperitoneum, the inferior mesenteric vein is ligated and excised early (**Fig. 4d and e**). The pancreatic tail is excised together with a part of the left perirenal fat. If the transverse colon can be preserved, care should be taken not to injure the arc of Riolan. Finally, en bloc resection is performed with the specimen as the module (**Fig. 5**).

From 2017 to 2019, we performed DP-TCR using the mesenteric approach for six patients with advanced pancreatic body and tail cancer who satisfied the surgical indications. The staging of pancreatic cancer was determined using the 8th Union for International Cancer Control (UICC) TNM classification<sup>15</sup>. Furthermore, to evaluate the cancer stump of the resected specimen and implement radical surgery, we used the criteria described in the Classification of Pancreatic Carcinoma, 4th English edition<sup>10</sup> and National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, Pancreatic Adenocarcinoma Version 1.2020<sup>11</sup>.

We recommend neoadjuvant chemotherapy or chemoradiotherapy for patients with a preoperative diagnostic classification of T4. This protocol was approved by the Ethics Committees of Nippon Medical School Musashikosugi Hospital (No. 5283157).

The distributions of two groups were compared with the Mann-Whitney U test and the chi-square test. Significance was defined as p < 0.05. JMP version 9.0.0 (SAS Institute, Cary, NC, USA) was used for statistical analysis.

# Results

DP-TCR using the mesenteric approach comprised DP-TCR alone in three patients, transverse colon resection and DP-TCR in one patient, and DP-TCR and celiac axis resection (DP-TCR-CAR) in two patients (**Table 1**). Regarding preoperative treatment, neoadjuvant chemoradiotherapy was administered to one patient who underwent DP-TCR-CAR (gemcitabine + 50 Gy) but was not administered to four patients. Furthermore, in the patient who underwent concurrent transverse colon resection, invasion of the retroperitoneal tissue and transverse colon with several disseminations in the omental bursa were observed at the initial examination. Therefore, as an unresectable pancreatic cancer, six cycles of chemotherapy using gemcitabine + S1 were administered, after which a partial response (Response Evaluation Criteria In Solid DP Using Mesenteric Approach



- Fig. 4 a: Skeletonization of the superior mesenteric vein was performed; however, the caudal side of the pancreatic body and tail on the left side of the superior mesenteric vein was not separated from the transverse mesocolon.
  - b: After dissecting the pancreatic neck, the remaining fusion fascia of Toldt was sectioned at the left side of the portal vein.
  - c: After sectioning the fusion fascia of Toldt, the anterior surface of the superior mesenteric artery was exposed. The pancreatic body, root of the transverse mesocolon, and retroperitoneal tissue of the right margin of the resected stump (area indicated by dotted line).
  - d: The root of the transverse mesocolon on the left side of the SMV was cut extensively (arrowheads).
  - e: The left perirenal fat was exposed, and the pancreas body and tail covered by the fusion fascia of Toldt was mobilized to the cranial side (arrowheads).

Tumor; RECIST)<sup>19</sup> persisted, and conversion surgery was indicated (**Fig. 6**).

The median operative duration was 258.5 (229-360) min, and median blood loss was 495 (150-1,110) mL for six patients who underwent DP-TCR. The median operative duration for the six patients who received standard DP (17 patients) over the same period was 195.0 (165-235) min. The median amount of blood loss was 357

(125-1,280) mL. Both the operative duration and amount of blood loss were significantly greater for DP-TCR (Mann-Whitney U test: p < 0.05).

An image of an entire resected specimen from Case 3 is shown in **Fig. 7a**. En bloc resection was performed from the main lesion margin to a distant site, including the transverse colon as the module. Observation of the sectioned surface on the cephalocaudal plane revealed

that the cancer with extrapancreatic invasion had invaded the retroperitoneum at the root of the transverse mesocolon in vertical and horizontal directions. Furthermore, direct invasion of the transverse colon was suspected (Fig. 7b). The sectioned surface A revealed the tumor center, extrapancreatic invasion of cancer cells, with tissue of mucinous adenocarcinoma extending to the fusion fascia of Toldt to the adipose tissue. The fusion fascia of Toldt was entangled midway and torn, making it difficult to observe (Fig. 7c). Furthermore, the tumor was enlarged and compressed but did not penetrate the fusion fascia of Toldt (Fig. 7d). It is important to note that retroperitoneal tissue with sufficient thickness to provide a vertical and horizontal margin was observed (Fig. 7c and d), which is a result of using the mesenteric approach. On the basis of histopathological examination, for cancer with extrapancreatic invasion, en bloc resection by DP-TCR was confirmed to contribute to ensuring DPM and PPM. Furthermore, in Case 3, there were multiple controlled local disseminations within the omental



Fig. 5 Completion of resection. En bloc resection of the resected organs, including the transverse mesocolon, was carefully completed.

bursa; however, all were resected using DP-TCR with concurrent resection of the transverse colon. Moreover, pathology results showed no viable cancer cells in any of the disseminated lesions in the omental bursa. The staging was stage IB in one patient, stage IIB in three patients, and stage III in two patients (UICC classification). In all patients who underwent DP-TCR, histopathological radical (R0) surgery, including both DPM0<sup>10</sup> and PPM-<sup>11</sup>, was possible. In this retrospective study, the histopathological radicality of distal pancreatectomy without DP-TCR for 15 patients with the same disease stage as the DP-TCR patients was 73% (chi-square test: p < 0.05).

No Clavien-Dindo grade IIIa or worse perioperative complications were observed in any patient. Furthermore, there was no significant difference in the rate of complications of postoperative pancreatic fistula, as compared with standard distal pancreatectomy. All patients completed adjuvant chemotherapy with S1, and the median postoperative observation period was 610 days. With regard to outcomes, hepatic recurrence was confirmed on postoperative day 595 in one patient who underwent DP-TCR-CAR. The patient declined chemotherapy and died on postoperative day 697. Furthermore, the patient who underwent conversion surgery developed intrapelvic peritoneal recurrence on postoperative day 470 and continues to receive chemotherapy with gemcitabine plus nab-paclitaxel. The other four patients are alive and recurrence-free.

## Discussion

The pancreatic body and tail has particular anatomical characteristics: 35 to 50 days after fertilization, the midgut rotates 270 degrees counterclockwise, and the dorsal side of the pancreas becomes the ventral side. There is thus no membrane boundary between the pancreatic body and tail with the transverse mesocolon. As a result,

Case	operation	OP time	BL	Т	N	М	stage	pathology	DPM	PPM	APS (S)	NAC	Adjuvant	recurrence	RFS	OS	out- come
1	DPTCR-CAR	366	1,110	4	1	0	111	tub	0	_	+	_	S1	+	595	697	dead
2	DPTCR	229	160	2	1	0	llB	tub	0	-	-	_	S1	-	_	629	alive
3	DPTCR+ colectomy	257	740	3	1	0	llB	muc	0	-	+	GEM+ S1	S1	+	470	622	alive
4	DPTCR	260	150	2	0	0	lB	tub	0	-	+	_	S1	-	-	597	alive
5	DPTCR-CAR	354	1,100	4	2	0	111	tub	0	-	+	GEM+ 50 Gy	S1	-	-	412	alive
6	DPTCR	235	250	3	1	0	llB	tub	0	-	+	_	S1	-	_	226	alive

Table 1 Characteristics of surgical patients

Abbreviations: OP, operation, BL, blood loss, NAC, neoadjuvant chemotherapy, RFS, recurrence-free survival, OS, overall survival



Fig. 6 CT image of Case 3 before the start of neoadjuvant chemotherapy. Extrapancreatic invasion of the main tumor is present, as is invasion of the fusion fascia of Toldt and deeper. Invasion of the transverse mesocolon and transverse colon is suspected (arrowheads). Furthermore, several disseminations within the omental bursa can be seen (arrows).



Fig. 7 a: Image of a complete resected specimen from Case 3. En bloc resection was performed up to a site away from the main lesion as the module.

- b: Macro-image of the sectioned surface of the main lesion. The tumor invades outside the pancreas, and marked shortening of the transverse mesocolon can be observed (are indicated by dotted line).
- \*Transverse colon.
- c: On the sectioned surface A, the tumor invades adipose tissue on the caudal side of the fusion fascia of Toldt. Arrowheads: fusion fascia of Toldt, arrows: Toldt fascia rupture (Elastica Masson-Goldner stain).
- d: On the sectioned surface A, the fusion fascia of Toldt extends from the dorsal side of the splenic artery (cranial side) toward the transverse colon and serves as a protective wall against the cancer. Arrowheads: fusion fascia of Toldt (Elastica Masson-Goldner stain).

when cancer of the pancreatic body and tail invades tissues outside the pancreas, it can easily invade the transverse mesocolon (Fig. 1a)<sup>5,20-22</sup>. Furthermore, the fusion fascia of Toldt is located at the dorsal side of the pancreatic body and tail in continuity with the anterior surface of the kidneys; even if the pancreatic body and tail spreads dorsally from the pancreas, the SMA, abdominal aorta, left renal vein, left adrenal gland, and other retroperitoneal tissue serve as a protective wall against invasion (Fig. 1b). Therefore, in patients with cancer confined to the pancreas<sup>6-9</sup>, a cancer-negative margin in the dissected peripancreatic margin (DPM0, PPM-) can be ensured if standard distal pancreatectomy is performed. However, when extrapancreatic invasion of cancer cells is present, the fusion fascia of Toldt, which serves as a protective wall, is penetrated, and invasion spreads further dorsally, resulting in DPM1 and PPM+, despite standard distal pancreatectomy, thereby making histologically radical surgery impossible. A procedure developed by Strasberg et al. to achieve further thorough dissection of the retroperitoneum in such situations17 involves antegrade en bloc resection of the retroperitoneal tissue extending from the pancreatic body toward the pancreatic tail and spleen, including the fusion fascia of Toldt, left adrenal gland, lymph nodes, adipose tissue, and nerve tissue dorsal to the pancreatic body and tail. This procedure, RAMPS, is performed extensively worldwide as the primary procedure for advanced cancer of the pancreatic body and tail<sup>23-26</sup>.

RAMPS and our proposed DP-TCR procedure aim to achieve histologically radical surgery. Both procedures have the same philosophy in that they involve an attempt to resect the retroperitoneum en bloc with the pancreatic body and tail and the spleen. However, our procedure differs greatly from that of RAMPS in that retroperitoneum deeper than the fusion fascia of Toldt is dissected first, and the transverse mesocolon to the left of the PV is resected en bloc, with the pancreatic body and tail as the module (ensuring the caudal margin).

The advantage of first dissecting the retroperitoneum deeper than the fusion fascia of Toldt is that the dorsal margin can be more accurately ensured by dissecting the dorsal infiltrative margin of the cancer tension-free. Furthermore, at the start of surgery, if the presence of cancer can be confirmed in the dissection stump in the deepest part of the retroperitoneum, unnecessary non-radical surgery can be avoided.

The advantage of concurrent resection of the transverse mesocolon is that for cancer invasion spreading laterally from the pancreatic body and tail (particularly in a cephalocaudal direction from the head to tail, ie, cancer invasion of retroperitoneal tissue in the root of the transverse mesocolon), DPM0 and PPM- can be ensured. For cancer of the pancreatic body, en bloc resection of the transverse mesocolon can be achieved by applying the mesenteric approach used in isolated pancreatoduodenectomy for advanced cancer of the pancreatic head<sup>12-14</sup>. The greatest advantage of the mesenteric approach is that the retroperitoneum dorsal to the fusion fascia of Toldt can be directly approached and that the transverse mesocolon can be systematically resected en bloc<sup>13,14,27,28</sup>. The report by Strasberg et al. does not mention a specific procedure for cancer invading toward the root of the transverse mesocolon.

None of the present patients who underwent DP-TCR underwent transverse colon resection because of poor blood flow to the transverse colon after specimen extraction. To avoid poor blood flow to the transverse colon, the marginal vessels should be accurately secured intraoperatively, and blood flow should be verified while performing experimental clamping of the proximal colic artery with bulldog forceps before commencing resection (**Fig. 2**). The fact that operative duration and amount of intraoperative blood loss were significantly greater in DP-TCR than in standard distal pancreatectomy was expected, given the significant difference in the degree of localized cancer progression (T factor) between the two groups.

The fact that all patients were DPM0 and PPM- demonstrated excellent local control by DP-TCR (**Table 1**). The proactive combined use of neoadjuvant chemotherapy and neoadjuvant chemoradiotherapy<sup>29-33</sup> should be addressed in the future. We believe that outcomes can be improved further by completing neoadjuvant chemotherapy and chemoradiotherapy, radical surgery, and adjuvant chemotherapy<sup>34,35</sup>.

Our study has several limitations associated with the errors and biases inherent to a small study, and future trials with larger numbers are recommended to further evaluate the effectiveness of DP-TCR for patients with pancreatic body and tail cancer.

#### Conclusion

We believe that DP-TCR is useful as a radical surgery for advanced pancreatic body and tail cancer with extrapancreatic invasions.

Conflict of Interest: The authors declare no conflicts of inter-

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