

ORIGINAL RESEARCH



Outcomes after combined right hemicolectomy and pancreaticoduodenectomy for locally advanced right-sided colon cancer: a case series

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Abstract

Background: Although right colon cancers mostly grow intraluminally, they may rarely invade neighboring organs without distant organ metastasis. En bloc resection is required for R0 resection in pancreas and duodenum-invasive right colon tumors. Despite the high mortality and morbidity rates, the en bloc right hemicolectomy and pancreaticoduodenectomy (RHPD) procedure can be safely performed in centers experienced in colorectal and hepatobiliary surgery. **Objective:** In this study, we aimed to share the results of our patients who underwent en bloc pancreaticoduodenectomy in addition to right hemicolectomy for cases with locally advanced right colon cancer. **Materials and Methods:** Patients who were operated on the right colon cancer between January 2010 and March 2018 were retrospectively screened. Patients who underwent RHPD due to locally advanced colon cancer invading the duodenum and pancreas were included in this study. RHPD was performed in cases where radical resection was deemed appropriate, and R0 resection could be performed. Demographic information, intraoperative and postoperative findings, and long-term follow-up data of the patients were recorded. **Results:** Six cases underwent RHPD. All of the cases were male, and the mean age was 67 ± 6 . Proximal PD was performed in five cases, and total PD was performed in one case. SMV reconstruction was performed in one case with an SMV invasion. One case died due to pneumonia and anastomotic leak in the postoperative period. The other five patients had a mean disease-free survival of 29.2 ± 14.7 months. The 1 and 2-year survival rate was 66.6% and 66.6%, respectively. **Conclusion:** RHPD is a surgical operation that can be performed safely in experienced centers with acceptable mortality and morbidity rates in cases suitable for R0 resection.

Keywords

Locally advanced right-sided colon cancer; Right hemicolectomy; Pancreaticoduodenectomy

1. Introduction

Adjacent organ invasion rate of colorectal cancers without distant organ metastasis varies between 5.2-23.6%, and adjacent organ invasion of right colon cancers is lower than the left colon and rectosigmoid cancers [1–3]. Although right colon tumors often show growth patterns intraluminally, they may invade the duodenum, pancreas, liver, gall bladder, right kidney and adrenal gland.

Locally advanced colon cancers are classified as T4 according to TNM staging [4]. In locally advanced colon cancers, incomplete resection of the tumor and residue in the adjacent organ are risk factors for poor prognosis and recurrence. En bloc right hemicolectomy + pancreaticoduodenectomy (RHPD), which was first proposed by Bacon and caused some discussions, has been defined as a critical prognostic

factor that prolongs survival in patients with R0 resection [5, 6]. Although the operation is a complicated procedure and includes a high risk of complications, today, it can be performed safely in experienced centers [1–4].

In this study, we aimed to share our experience with RHPD cases that were operated on with the diagnosis of locally advanced right colon tumors invading the duodenum and pancreas.

2. Material and method

Colorectal surgical operations performed between January 2010 and March 2018 and were reviewed retrospectively in this study. Patients with locally advanced right colon cancer who underwent right hemicolectomy with proximal pancreaticoduodenectomy or total pancreaticoduodenectomy

were included in this study. Cases with recurrent colon cancer, distant organ metastasis, or peritonitis carcinomatosa were excluded from this study. Ethical approval was obtained to conduct this study. En-bloc multivisceral resection was performed in patients with RHPD to provide a negative surgical margin. The operation decision in all patients was made by the multidisciplinary oncology council. Patients were subjected to the ECOG performance scale. Patients with an ECOG performance of 0-1 were deemed appropriate for this surgical treatment. This surgical treatment was performed with a joint decision after discussion with the patients and their relatives. Gastro-duodenoscopy and colonoscopy were performed on all preoperative patients, the biopsy was taken, and the colon cancer diagnosis was made histopathologically. Preoperative contrast-enhanced computed tomography (CT) was routinely performed in all patients to evaluate local tumor invasion to neighboring organs, and the opinions of two expert radiologists were obtained. The en-block radical resection margin was determined for invasive organs. All data for patients were analyzed retrospectively from the hospital database. Patient demographic information, operation method, operation time, intraoperative bleeding amount, histopathological findings (tumor type, tumor size, invasion depth, lymph node invasion), postoperative follow-up results (length of stay, complications, mortality), oncological follow-up results (chemotherapy status, disease-free survival time) was recorded. The mortality that occurred during the postoperative admission period or within 30 days was accepted as perioperative mortality.

2.1 Surgical method

After the Cattell-Braasch maneuver was performed to mobilize the colon and provide sufficient exposition, the duodenum was mobilized with the Kocher maneuver. In the next step, the right colon resectability, duodenal, and/or pancreatic invasion were evaluated. After confirming that radical resection was feasible and that R0 resection could be performed, right hemicolectomy and pancreaticoduodenectomy with concurrent sessions were performed. First of all, right hemicolectomy was performed under the standard oncological procedure. Then, in the standard procedure, pyloric-sparing pancreaticoduodenectomy was performed. If there is a superior mesenteric vein (SMV) invasion, en bloc SMV resection with Satinsky clamps followed by SMV reconstruction was performed. Since the SMV invasion was under 2 cm, end-to-end anastomosis was performed with a continuous suture. The end-to-end duodeno-mucosal anastomosis was performed between the proximal stump of the pancreas and the jejunum. Routinely, pancreaticojejunostomy was performed over a stent placed in the pancreatic canal. Hepaticojejunostomy and gastrojejunostomy procedures were performed, respectively. Finally, side by side isoperistaltic ileotransversostomy was performed with the help of a linear stapler. After the reconstruction procedures, rubber drains were placed next to the biliary and pancreatic anastomoses, and the abdominal incision was closed.

2.2 Follow-up system

All patients were checked at 3-month intervals in the post-operative period. Patients were followed up according to a standard protocol that consists of carcinoembryonic antigen (CEA), CA19-9 measurement, abdominal CT, and annual colonoscopy.

3. Results

In 10 of 1613 colorectal surgery operations performed in our clinic, simultaneous pancreaticoduodenectomy was performed due to pancreas and duodenum invasion. Three patients were excluded because of benign disease. Colon adenocarcinoma was detected in six patients as a result of biopsies taken by colonoscopy. In cases 1 and 3 referred to in Table 1, signs of external compression in the first segment of the duodenum were observed in gastroduodenoscopy. The demographic information of the patients is given in Table 1. All patients were operated on electively. Only one of the patients received neoadjuvant chemotherapy, and all patients who survived post-operatively were administered adjuvant chemotherapy. CEA and CA 19-9 levels are shown in Table 2.

En bloc right hemicolectomy plus total pancreaticoduodenectomy was performed in one of the patients, and right hemicolectomy plus proximal pancreaticoduodenectomy was performed in five patients. The mean operation duration was 332.5 ± 42.9 minutes, intraoperative bleeding was 1483.3 ± 248.3 cc, and the mean hospital stay was 31.2 ± 10.6 days (Table 2).

Pancreatic fistula developed in two patients and delayed gastric emptying was observed in two patients. Oral intake was stopped in Case 6, who developed a pancreatic fistula. Total parenteral nutrition and somatostatin treatment were initiated. The pancreatic fistula was closed on the 8th postoperative day. Case 1 with pancreatic fistula died. The average disease-free survival time was 29.2 ± 14.7 months (Table 2). The 1 and 2-year survival rate was 66.6% and 66.6%, respectively.

Histopathological examination revealed mucinous adenocarcinoma in four cases, cribriform and 20% tubular adenocarcinoma (mixt) form in two cases.

In preoperative abdominal CT, fatty planes between the colon and pancreas/duodenum were observed in all patients. In Case 3, radiological invasion of the duodenum and pancreas, as well as an invasion to the gallbladder, was observed, but no tumor was observed in the gallbladder margins in the histopathology of the specimen. Three patients had duodenum invasion, whereas three patients had duodenum and pancreatic invasion. R0 resection was performed in six cases, and R1 resection was performed in one case. Tumor volume was, on average, 108.5 ± 66.2 cm³. A mean of 35.6 ± 8.4 lymph node excisions was performed, and all patients had lymph node metastasis (minimum 1, maximum 8) (Table 1).

TABLE 1. Demographic, operational, pathological and postoperative data.

	Demographic		Operational findings					Pathological findings				
	Gender	Age	Operation	Op. Time (minute)	Bleeding (cc)	Complication	Clavien Dindo classification	Pathology	Invasion	Resection	Tumor size (cm)	LN status (n)
Case 1	M	73	RHTPD	330	1400	pneumonia, pancreatic fistula	V	Mucinous adenocarcinoma	Duodenum	R0	7,5×5,5×1,5	31/8
Case 2	M	65	RHPPD +SMV recons	360	1900	no	-	80% cribriform-20% tubular adenocarcinoma	Duodenum and pancreas	R0	6×3,5×4	32/5
Case 3	M	57	RHPPD	280	1500	no	-	Mucinous adenocarcinoma	Duodenum and pancreas	R1	8×12×2,5	52/1
Case 4	M	66	RHPPD	325	1300	delayed gastric emptying	I	80% cribriform-20% tubular adenocarcinoma	Duodenum	R0	6×3,5×5	29/4
Case 5	M	68	RHPPD	400	1200	delayed gastric emptying	I	Mucinous adenocarcinoma	Duodenum	R0	5×3×6	34/2
Case 6	M	73	RHTPD	300	1600	pancreatic fistula	IIIa	Mucinous adenocarcinoma	Duodenum and pancreas	R0	7×5×2	36/8

M: Male, RH: Right hemicolectomy, TPD: Total pancreaticoduodenectomy, PPD: Proximal pancreaticoduodenectomy, SMV: Superior mesenteric vein. Recons: Reconstruction, Op.: Operation, LN: lymph node.

TABLE 2. Follow-up results of the patients.

	Preop CEA levels (ng/mL)	Postop 6th month CEA levels (ng/mL)	Hospitalization	Preop CA 19-9 levels (ng/mL)	Preop CA 19-9 levels (ng/mL)	Neoadjuvant / adjuvant chemotherapy	Survival (months)	Mortality
Case 1	48	-	49	77	-	no/-	ex	yes
Case 2	26	18	26	69	20	no/yes	40	no
Case 3	55	56	20	41	35	no/yes	31	no
Case 4	34	7	36	45	10	yes/yes	6	no
Case 5	24	4	23	34	11	no/yes	43	no
Case 6	126	28	33	86	16	no/yes	26	no

4. Discussion

Right colon cancers cause relatively less neighboring organ invasion among colorectal cancers. Adjacent organ invasion rate of locally advanced right colon cancers has been reported between 11-28% [1]. The most common structures invaded by right colon tumors have been reported as the peritoneum, 25% abdominal wall, 16% omentum, 16% small intestine (excluding duodenum), and in rare cases 4% uterus 3% duodenum 2% Gerota fascia [7]. Mostly, a cure cannot be provided in tumors with neighboring organ invasion [8]. In colorectal cancers, even if distant organ metastases are present, a cure can be achieved [9].

Thanks to the advancement in CT technology, lymph node and distant organ metastases can be evaluated with high accuracy and the diagnosis of locally advanced colon cancer can be made preoperatively [2, 10]. Distant organ metastasis (especially liver metastasis) and T4 stage can be detected at a high rate with CT, but peritonitis is insufficient in detecting carcinomatosis [4, 10]. CT may be insufficient to distinguish between metastatic adhesion and inflammatory reaction. This challenging separation may lead to confusion even during the operation [4, 11]. Definitive diagnosis can only be made by histopathological examination [11]. In the histopathological examination of the adhesions detected during the operation, malignancy was present in 50-94% [2, 4, 12, 13]. Therefore, adhesions detected intraoperatively should be considered as malignant lesions [14]. Although endoscopy helps in determining the duodenal invasion of right colon cancers, only in cases with serosa invasion, the duodenal mucosa can be seen as completely normal [11]. All cases in our study had a suspicion of duodenal and/or pancreatic invasion in the preoperative CT examination. In our multidisciplinary oncology council, an operational decision was made for all cases.

Although partial duodenectomy is recommended for right colon tumors with a comorbid disease or elderly patients without the invasion of ampulla vateri, the importance of en bloc resection emerges as the local recurrence rate is high [1, 4, 15]. Satisfactory results can also be obtained in elderly patients [16]. Therefore, en bloc resection is increasingly recommended by authors in the right colon tumors without distant organ metastasis [17].

Local recurrence rate has been reported to be 70-100% when en bloc resection cannot be performed [1-4]. Some authors argue that it is not the most appropriate treatment option due to the local recurrence rate, the difficulty and complexity of the operation, high mortality and morbidity rates, and high cost [18]. Therefore, in cases with intraoperatively detected neighboring organ invasion, if the surgeon does not have sufficient experience, it is recommended to terminate the operation and refer the patient to an experienced center [13]. En bloc resection was successfully performed in all RHPD operations performed in our center.

Although mortality and morbidity rates have decreased with surgical techniques and technological developments, RHPD is still a controversial operation [19]. In the RHPD operation, which is a complicated procedure, five anastomoses are performed. The anastomotic leak rate due to this procedure was reported as 39.8-50%, and the mortality rate was 5% [8]. In our

patients, the rate of anastomotic leakage was 33.3%, and the mortality rate was 16.6%. Given the challenge of the operation and a large number of anastomoses, it can be considered as acceptable rates.

Neoadjuvant chemo-radiotherapy or intraoperative radiotherapy is another option in locally advanced cancers. It decreases the local recurrence rate and allows R0 resection. Especially neoadjuvant chemotherapy decreases its stage by 55% and reduces the tumor volume by 62.5% [1, 2]. It has been reported that adjuvant chemotherapy reduces recurrence and prolongs survival rates in lymph node-positive patients [20]. Only Case 4 from the patients in our study received neoadjuvant chemotherapy treatment, and all patients received adjuvant chemotherapy. By the decision of the surgical oncology council in experienced centers, in cases with locally advanced right colon cancer, which does not include distant metastasis or carcinomatosis peritonei, this operation, with or without neoadjuvant chemotherapy, is a treatment option depending on patient performance. In the literature, case series have been reported without neoadjuvant chemotherapy [1, 2]. With an experienced surgical team, there is an opinion that the postoperative mortality and morbidity rates of en bloc pancreaticoduodenectomy and right hemicolectomy are non-inferior to other treatment methods. Although this complex operation can be performed without administration of the neoadjuvant chemotherapy in experienced centers, we recommend preoperative neoadjuvant treatment given that neoadjuvant chemotherapy reduces cancer stage and size.

Another important prognostic factor is the lymph node invasion [1]. In some studies, it has been stated that en bloc resection can prolong survival regardless of lymph node invasion [11]. It has been reported that 5-year surveillance in patients with R0 resection is between 21-60% and disease-free survival time is between 16-54 months [21]. Some studies have reported that the survival of patients with negative lymph nodes is longer than patients with positive lymph nodes and that patients with lymph node-negative survive for more than seven years [2, 22, 23]. In our cases, to reach R0 resection, SMV resection was performed in addition to RHPD in two patients, and lymph node metastasis was detected in all patients. Therefore, we could not evaluate the effects of lymph node metastasis on survival in our study. The overall survival of our patients was, on average, 29.2 ± 14.7 months.

The low number of patients is the most important limitation of our study. The reason for this is that locally advanced right colon cancers invading the pancreas and duodenum are extremely rare. In addition, there are very few patients suitable for RHPD operation. Larger studies can provide more reliable results. However, this study has some strengths. First of all, all patients were followed up, and their prognoses were determined. Also, preoperative CT findings, surgical exploration findings, and histopathological examination results of all patients were presented in detail. The reason for the short postoperative survival time in Case 4 is due to death because of myocardial infarction. Case 1 died due to surgery complications. For this reason and because of the small number of cases, survival time between patients who received and did not receive neoadjuvant chemotherapy could not be compared. There are quite few studies on this subject in the past five years

in the literature.

In conclusion, although RHPD in locally advanced right colon cancer is an operation with high mortality and morbidity in patients suitable for R0 resection, it can be successfully performed in experienced centers and prolongs survival. There is a need for larger, long-term, randomized studies on this aggressive surgical procedure.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Local Human Ethics Committee (14/09/2020-11895).

AUTHOR CONTRIBUTIONS

Concept – S.S.U., O.A., A.K.Z.; Design - S.S.U., O.A., A.K.Z.; Supervision –A.N.S., D.E.T.S., A.K.Z.; Resource – S.S.U., O.A.; Materials - S.S.U., O.A.; Data Collection and/or Processing - S.S.U., A.N.S.; Analysis and/or Interpretation - S.S.U., A.N.S., D.E.T.S.; Literature Search - S.S.U., A.N.S., D.E.T.S.; Writing - S.S.U., A.N.S., D.E.T.S.; Critical Reviews - S.S.U., A.N.S., O.A., A.K.Z.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

INFORMED CONSENT

Written informed consent was not necessary because no patient data have been included in this manuscript.

HUMAN RIGHTS

This study was conducted according to the World Medical Association Declaration of Helsinki.

AVAILABILITY OF DATA AND MATERIALS

The materials described in this manuscript will be freely available to any scientist wishing to use them for non-commercial purposes without breaching participant confidentiality.

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