Colo-pancreaticoduodenectomy for Locally Advanced Colon Carcinoma- Feasibility in Patients Manifesting as Acute Abdomen

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Abstract

Background

The only curative option for locally advanced colon carcinoma invading duodenum and/or pancreatic head is the en-bloc right hemicolectomy plus pancreaticoduodenectomy (PD), so called colo-pancreaticoduodenectom (cPD). Patients with this disease may present as an acute abdomen. Emergent PD often has high postoperative morbidity and mortality. Here we aimed to evaluate the feasibility and outcomes of emergent cPD for such patients of advanced colon carcinoma, manifesting as life-threatening acute abdominal conditions.

Patients and Methods

We retrospectively review of 4,793 patients who underwent curative colectomy for the treatment of colorectal cancer in the period from 1993 and 2017. Among these patients, 30 had locally advanced right colon cancer and underwent a cPD. The cPD of 11 patients were performed in acute abdomen conditions (bowel obstruction 6, perforation 3, tumor bleeding 2). Selection criteria for emergent cPD were: (1) age ≦60 years, (2) body mass index <35 kg/m^2, (3) no poorly-controlled comorbidities, and (4) perforation time ≤6 hours. Three patients who failed to meet these criteria received non-emergent cPD after a life-saving diverting ileostomy, and cPD was performed three months later. The patients clinicopathological characteristics, the early and long-term postoperative outcomes were compared between emergent cPD (e-group, n=11) and non-emergent cPD (non-e group, n=19). After cPD, staged pancreaticojejunostomy (PJ) was performed in all e-group, and on 15 of 19 non-e group patients.

Results

The non-e group had significant higher patient age and higher incidence of associated comorbidities, while clinicopathological characteristics were otherwise similar. None of the patients in the two groups succumbed from cPD. Postoperative complication rate was 63.6% in the e-group, and 42.1% in the non-e group (p=0.449). The 5-year overall survival rate was 15.9% in the e-group, and 52.6% in the non-e-group (p=0.192).

Conclusions

In highly selected patients, emergent cPD is feasible by cooperation of experienced colorectal and pancreatic surgeons. The early and long-term outcomes of emergent and were similar to those after non-emergent cPD.

Introduction

The prevalence of colorectal carcinoma (CRC) is increasing worldwidely (1). In Taiwan, this maligancy constantly ranked annually as the largest number of new malignancy cases during the past 2 decades (2). The only hopeful cure is radical colectomy in the early stage to obtain an R0 resection (3).

For locally advanced CRC, en-bloc resection of involved adjacent organ is necessary (4). However, multi-organ resection for CRC often have higher postoperative morbidity and mortality (3–5).

When a right colon cancer directly infiltrates the duodenum near the ampulla of Vater or pancreatic head, radical resection procedures include a right hemicolectomy plus pancreaticoduodenectomy (PD), which we named here colo-pancreaticoduodenectomy (cPD)(5–25).

On the other hand, Kausch in Germany and Whipple in USA demonstrated first the brief techniques of PD during the early 20th century. This operation procedure is also known as the “Kausch-Whipple operation” (26) for treating neoplasms or complex injuries or diseases involving duodenum and pancreatic head (26–34). Recently, despite the lowered operative mortality of PD to <5%, its complication rate remains high (up to > 40% in the recent literatures)(26–34). The complexity of cPD is even greater over PD, and cPD further has higher operative morbidities and mortalities (5–25). Moreover, PD performed during emergency condition also are more risky (20, 27–31, 33). Operative mortality related to emergent PD exceeds 20 to 40% (20, 27–31, 33). Patient’s preoperative condition and its PD etiology are important factors affecting safety issues of emergent PD (29–31, 33).

Emergent resection of a bowel tumor is indicated for patients with causes bowel obstruction, perforation or tumor bleeding (32). Our hospital is the only government-supported public, tertiary referral medical center in central Taiwan. We occasionally encountered such patients manifestation as life-threatening conditions of CRC. Few studies have so far reported on the emergent cPD for locally advanced CRC patients at critical acute abdominal conditions (31, 32). Here, we retrospectively reviewed our patients with the aimed to evaluate the feasibility and value of emergent cPD for locally advanced CRC patients showing acute abdomen.

Patients And Methods

Between a period of 25 years (from 1994 to 2018) our hospital admitted 4,898 patients for radical curative resection for CRC. Among them, 30 patients had locally advanced CRC infiltrating duodenum and/or pancreatic head and underwent cPD. Of these 30 patients, 11 received cPD under emergent conditions (e-group). Their detailed information is shown in Table 1. Their causes of emergent cPD are the following: acute bowel obstruction in 6, tumor perforation after colonoscopic tumor biopsy in 2, spontaneous tumor perforation in 1, and tumor bleeding in 2.

Table 1
Brief data of patients who underwent emergent colo- pancreaticoduodenectomy

Case no.	Sex	Age	Serum CEA Level (ng/ml)	Cause of emergency	Comorbidity	PD procedure	Complications	Hospital stay (days)	Operatie blood loss (ml)	Total B.T (ml).	Present status
1	M	59	11.4	iatrogenic perforation		PPPD	Wound infection, POPF (B)	28	1100	1000	DOD, 16 m
2	M	59	2.3	iatrogenic perforation		PD	DGE(B)	33	550	0	NED, 34 m
3	F	66	1.7	tumor bleeding	Diabetes mellitus	PPPD	DGE(A) BPC	27	600	500	DOD, 14 m
4	M	50	61.2	bowel obstruction		PD		19	1000	2100	DOD, 52 m
5	F	44	369	bowel obstruction		PD		22	800	2600	DOD, 27 m
6	F	36	1.0	Spontaneous perforation	Lupus erythematosus	PPPD		11	500	0	NED, 68 m
7	F	50	63.4	bowel obstruction		PD	Bowel abscess, DGE (A)	74	600	0	DOOD, 54 m
8	M	43	1.6	bowel obstruction		PD		8	500	0	NED, 120 m
9	M	52	19.8	bowel obstruction		PPPD	Biliary leak (A) abscess	13	600	0	NED, 49 m
10	M	52	14	bowel obstruction		PPPD	BPL Wound infection	16	500	0	DOD, 46 m
11		53	19	tumor bleeding		PPPD	Wound infection	16	0	0	DOD, 52 m

Note: PD: pancreaticoduodenectomy; PPPD: pylorus-preserving pancreaticoduodenectomy;

NED: no -evidence of disease; DOD: died of disease; DOOD: died of other disease; DGE: delayed gastric empting time; POPF: postoperative pancreatic fistula; BPL: biochemical pancreatic leakage.

During the same 25-year period, a total of 742 PDs were performed in our hospital. Those patients whose cPD was not performed due to locally advanced CRC or for other diseases were excluded for the present analysis (e.g., pancreatic head tumors with invasion to colon or mesocolon, or simultaneous resection of colon tumor and periampullary tumors, or complex injuries of colon and periampullary organs). Also, those with locally advanced CRC to duodenal wall with well-preserved ampullary area not indicated for cPD (9) were also excluded from this study. The choice of classical PD or pylorus preserving PD (PPPD)(26) was made based on the subjective judgement of a gross negative margin present at the duodenal wall.

A senior hepato-bilio-pancreatic surgeon (CCW) performed or guided all 742 PDs during the study period. All perioperative assessments and operative procedure of cPD were performed by senior surgeons (CCW and FKP), while strategies of colon cancer resection were determined by colorectal surgeons (JBC and CCC), and physicians CHC and YY designed chemotherapies and target therapies for CRC.

For emergent cPD done on patients with obstruction and perforation, their selection criteria are: (1) patient's age ≤60 years (2) body mass index < 35 kg/m^2, (3) no poorly-controlled comorbidities in perforation cases, the estimated perforated duration ≤6 hours without severe intra abdominal contamination. The other 19 patients (non-e group) whose cPD was performed under an elective regular schedule after well-examined preoperative studies.

Two initially diagnosed perforation cases and one obstruction case whose general condition did not meet the criteria outlined above, received diverting ileostomy with omental patch obliterating perforation holes. The other older patient with tumor obstruction was initially treated by diverting ileostomy. cPD of these three patients were performed three months later. These three patients were categorized in the non-e group.

Before elective cPD, all 19 patients in the non-e group received functional examinations of lung, heart, liver and kidney. Their comorbidities were well controlled. Their carcinoembryonic antigen (CEA) were checked. Computed tomography (CT) or magnetic resonance imaging (MRI) were performed.

For their reconstruction of pancreatic remnant to the gastrointestinal tract, pancreaticojejunostomy (PJ) was the main choiced procedure. In 4 non-e group patients, it was performed by the invagination method at the early years of this study (prior to March 1996). The following 15 patients in the non-e group, and all patients in the e-group. Staged PJ were performed (30, 35, 36) three months after cPD. Any complication or death occurring within 90 days after cPD were recorded as surgical complication or mortality. Complication severity was graded using Dindo-Clavien classification (37). The definitions and severity of pancreatectomy-related complications were followed those of the international study group of pancreatic surgery (ISGPS). They included postoperative pancreatic fistula (POPF)(38), postpancreatectomy hemorrhage (PPH)(39), delayed gastric empty (DGE) (40) and bile leakage (41), which were all used to grade the severity of pancreatectomy-related morbidities. After patients had recovered from cPD, they were followed-up at outpatient clinic on a monthly basis during the first year, and at intervals of 3–6 months thereafter. On each visit, CT or MRI was performed, and serum CEA levels measured.

Chemotherapy or targeted therapy were routinely administered after cPD for a minimum of two years. All patients were followed-up until July 2020.

Resected specimens were sent to the pathologist (YAC) to determine the pathological characteristics and cancer stages of CRC. The definition by the World Health Organization (WHO)(42) was used for cancer cell differentiation and AJCC (8th edition)(42) was used for cancer staging. The clinicopathological characteristics, early postoperative and long-term results after cPD of the patients in both groups were then compared.

Statistical Analysis

Continuous variables were presented as median (range), and compared using Mann-Whitney U test. Frequencies were compared using Fisher's exact test or Pearson's χ^2 test as appropriate.

The rates of overall survival (OS) until July 2020 were calculated using Kaplan-Meier life table method and compared using log-Rank test. Differences with values of $p < 0.05$ were regarded as statistically significant.

Results

All operations of cPD were performed by open laparotomy.

Table 2 compares background characteristics of patients in both groups. Higher ages and higher incidence of associated comorbidity were found in the non-e group. No differences was found with other variables. Comorbidities of 12 patients in the non-e group patients were old stroke in 2, rheumatoid arthritis in 1, coronary artery disease in 2, hypertension in 3, obstructive lung disease in 2, diabetes mellitus in 3, end-stage renal disease in 1 and chronic hepatitis in 1. (4 patients had ≥ 2 comorbidities).

Table 2
The clinical pathological characteristics of patients who underwent colectomy and pancreaticoduodenectomy

Clinical characteristics	e group(n = 11)	Non e group(n = 19)	p
Sex			
Male	7	8	0.449
Female	4	11	
Age(yr)	52(36.1–66)	70(46–86)	< 0.001
Associated comorbidities	2	12	0.039
Serum CEA level (ng/mL)	11.4(1.0-369.0)	8.0(1.5–3498.0)	0.726
BMI(kg/m^2)	23(20.5–31)	22.5(19.6–30.5)	0.776
Tumor characteristics			
Tumor size(cm)	7.5(3.0–11.0)	7.5(4.3–16.0)	0.331
Cancer differentiation			
Moderately diff.	4	9	0.631
Poorly diff.	7	10	
Depth of cancer invasion			
T4a(serosa)	3	2	0.327
T4b(adjacent organ)	8	17	
Lymph node metastasis	9	10	0.671
Dissected lymph node number	19(13–46)	24(15–69)	0.294
BMI: Body mass index; diff.: differentiated.			

Table 3 shows the early postoperative results after cPD. No patients succumbed from cPD in both groups. Rates of complication were high in both groups with no significant differences (e group 64% vs. non-e group vs. 42%, p = 0.449).

Table 3
Early postoperative outcomes after colectomy and pancreaticoduodenectomy

Early outcomes	e group(n = 11)	Non e group(n = 19)	p
PD type			
classical PD	6	9	0.867
PPPD	7	7	
Operative time (hour)	8.0 (5.5–10.9)	7.5 (6.2–11.8)	0.746
Operative blood loss (ml)	600 (400–1100)	420 (150–3130)	0.268
Blood transfusion (ml)	0 (0-2600)	0 (0-2250)	0.955
Need for blood transfusion (No)	4	6	0.677
Complication	7 (63.6%)	8 (92.1%)	0.449
wound infection	3	1	
intraabdominal abscess	2	2	
POPF grade B + C	2	2	
DGE	3	3	
PPH	0	1	
Grade B + C	0	1	
Dindo-Clavien severity grade 3 + 4	1	4	
Postoperative hospital day (days)	23 (18–74)	19 (9–45)	0.331
90-day mortality	0	0	1.000

PD: pancreaticoduodenectomy; PPPD: pylorus-preserving pancreaticoduodenectomy. POPF: postoperative pancreatic fistula; DGE: delayed gastric empting; PPH: postpancreatectomy hemorrhage.

One patient in the non-e group had dehiscence of an invaginated PJ (grade C POOF) with gastroduodenal artery stump bleeding (grade C PPH). He was rescued by an emergent total separation and closure of both pancreatic and intestinal stump, peripancreatic irrigation and total parenteral nutrition (43, 45). He developed a chronic pancreatic fistula which was treated with fistulo-jejunostomy (44) 6 months later.

Figure 1 shows the OS rates of the two groups, with no significant differences between them (p = 0.192).

Discussion

We reviewed our 25-year long experience on cPD for locally advanced colon cancer. The procedure of cPD is rarely performed procedure in gastrointestinal surgery. A nationwide survey in Netherland showed that the most common indication of cPD is locally advanced pancreatic head cancer (23) directly invading colon or mesocolon, followed by locally invaded colon cancer with duodenum and/or pancreatic head.

In 1998, surgeons in Sloan-kattering memorial cancer center commented that esophagectomy, hepatectomy, pancreatectomy and total pelvic exenteration are the most complex surgical procedures in cancer surgery (45). These procedures are recommended to be done in high-volume well-experienced medical centers. From our findings, we found that the postoperative courses of cPD were very similar to those after PD. Therefore, achieving a successful emergent cPD may be similar to ensuring a successful emergent PD. Emergent PD is associated with high postoperative morbidity and a high mortality usually > 30% (30–33).

However, Gulle et al (29) operated on 10 patients with emergent PD to treat complex pancreaticoduodenal trauma with zero death. All their patients were relatively young and healthy without associated troublesome co-morbidities. The risks of emergent PD for non-trauma patients are usually higher than trauma cases, because these patients usually have unrecognized preoperative poor conditions and ill-controlled co-existed inflammation or organ dysfunction that resulted in a failed emergent PD (30, 31, 33).

Managing postoperative complications after emergent cPD equally important as treating complication after emergent PD. The cPD is a challenging procedure, and is highly technique-demanded and time-consuming. It requires meticulous and experienced care during the

periperative period in order to reduce complication and death rates. Thus, the general preoperative conditions of patients should be well-surveyed to cope with potential postoperative adverse events. Therefore, criteria of preoperative patient selection are key to the cPD success.

Patients of older age, poorly controlled comorbidities, or obesity which typically are risks of PD were therefore excluded from our emergent cPD_surgery in treating bowel obstruction or perforation. Moreover, if the perforation time is long (> 6 hours), severe intra-abdominal contamination could lead to edematous and fragile conditions. Long periods of generalized peritonitis may cause easily breakdown of sutures in early postoperative period of cPD. Such patients are therefore not recommended for emergent cPD.

Acute massive bleeding from gastrointestinal malignancies is very rare but grave. Once that occurs, emergent resection to stop bleeding is likely the only life-saving option. The aforementioned patient selection criteria for obstruction and perforation cannot be totally applied indiscriminately in bleeding cases. Trans-arterial embolization may be transiently helpful for hemostasis (29, 46). However, due to abundant vascular collaterals in pancreaticoduodenal regions, total hemostasis is challenging. Bleeding tumor resection is still mandatory after hemostasis controlled by embolization.

Tsai et al. reported that intraperitoneal infections worse outcomes more than bleeding in emergent PD (33). In this series, we recommended 2 stage PJ after cPD.

PJ has been considered as the Achilles tendon of PD. For success of cPD, the management of PJ is also important. At the early period of our study (March, 1996), we had a case of grade C catastrophic POPF with PPH (disruption of PJ with massive internal bleeding). The patient fortunately survived after timely and appropriate management to overcome this diasterouse complication.

Intraoperative management for technique-related and technique-unrelated adverse events of cPD should be also be great concerns, to reduce chances of operative mortality.

Staged PJ was routinely used for all PD after this case when the pancreatic duct diameter is small (< 2 mm), pancreatic parenchyma is soft or associated with large vessel resection or controlled troublesome comorbidity. Staged PJ was firstly propose by Japanese surgeons, Miyagawa and Makuuchi in 1994 (39). They covered the common hepatic each proper hepatic arteries, and gastroduodenal artery stump using a sheet of pedicled greater omentum or liver falciform ligament (35, 36). Then, a thin plastic tube was inserted into the main pancreatic duct to totally exteriorize the pancreatic juice. The pancreatic juices was fed into intestine lumen through another tube jejunostomy. The seromuscular sutured to the posterior wall of the pancreatic stump. PJ was performed three months later by inserting the aforementionally placed plastic tube into the neighboring jejuna lumen.

The pedicled falciform ligament of the liver, or greater omentum is able to cover the transected stump of gastroduodenal artery (the most common site of PPH after PD). These vessels can be protected from erosion of leaked pancreatic juice. Actually, PJ is not the end of PD. No catastrophic complication had occurred in our patients after using 2-stage PJ procedures quaranteeing the safety of cPD.

The experience of treating acute necrotizing pancreatitis is also useful for treating POPF after PD (46). An appropriate and timely managements of complications after PD could improve healing and avoid operative death. The procedure of completion pancreatectomy for disruptured PJ (28) has high death rate (28, 40). Even with the development of chronic pancreatic fistula, treatment by fistulojejutnosomy can be effective without sequelae (44).

DGE is also a trouble adverse event of PD or cPD. The problem is likely due to the destruction of upper abdominal autonomic nerve fibers during the lymphadenectomy. The condition often requires prolonged hospitalization, long-term nasogastric decompression and total parenteral nutrition support. These managements could cause other systemic problems, such as catheter sepsis, electrolyte unbalance, trace elements deficiency, aspiration pneumonia and hepatic dysfunction. Some of them are fatal. To avoid such formidable complications, efforts to preserve the upper abdominal vagus nerve and sympathetic nerve plexus, can minimize chances of DGE. Upper abdominal lymphadenectomy, which is typically carried out for periampillar or pancreatic cancer, is not needed in CRC patients.

The 5-years OS for locally advanced CRC is 51%. The reported 5-year OS rate after cPD for locally advanced CRC is around 50–60% (26). Our non-e group patients prognosis is comparable to other literatures (4–11). Because of the high incidence of lymph node metastasis, e-group patients prognosis is somewhat poorer. Nevertheless, both groups had insignificantly different OS. Histological TNM staging, lymph involvement and cancer cell differentiation are prognostic factors (5–12, 14, 15, 17–21, 23–25). The cancer condition of our patients who undergoing cPD were similar to other literatures on patients of colon cancer. Development of new target agents or chemotherapeutic drugs may be helpful to prolong survival time after cPD.

Several limitations of current study are listed below.

First, this is a long-duration observational cohort study. It is not a randomized-controlled trial because of the small sample size. The CRC which involves duodenum and /or pancreas is a unique presentation. During the 25-year long duration of our study, diagnosis tools, surgical

techniques, operative equipments, and peri-preoperative assessments have markedly improved. Thus, our initial case-selection criteria in the e-group may have been too conservative. For example, the patient age can be extended as the life expectancy of the general population has increased by 5 years during this study period (47). The safety range of emergent cPD may also be extended.

Second, treatment strategies for locally advanced CRC were decided by experienced colorectal and hepato-pancreatico-biliary surgeons, and oncologists. These staff have turned over during this period. Although a senior surgeon (CCW) constantly has led the treatment strategy of individual patients, discrepancy in management in this complex disease remains. For example, the adjuvant therapies after elective or emergent cPD may differ because of different postoperative course.

Third, although staged PJ may ensure the safety of cPD, additional admission and operations are needed to complete PJ of patients. If we have had new safe guarded techniques on PJ, the safety of cPD with one single operation could have been developed, reducing both hospital costs and anesthetic risks.

Despite high complication rates, our reviewed experiences supported that emergent cPD is a feasible procedure on the highly selected patients with locally advanced CRC presenting as acute abdomen. The long-term outcomes after emergent and non-emergent cPD are comparable.

Conclusions

In highly selected patients, emergent cPD is feasible by cooperation of experienced colorectal and pancreatic surgeons. The early and long-term outcomes of emergent and were similar to those after non-emergent cPD.

Abbreviations

CRC: colorectal carcinoma; PD: pancreaticoduodenectomy; cPD:colo-pancreaticoduodenectomy; PPPD: pylorus preserving PD; CEA: carcinoembryonic antigen; CT: Computed tomography; MRI: magnetic resonance imaging; PJ: pancreaticojejunostomy; ISGPS: international study group of pancreatic surgery; POPF: postoperative pancreatic fistula; PPH: postpancreatectomy hemorrhage; DGE: gastric empty.

Declarations

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Authors' contributions

Wu CC and Chen JB conceived and designed the study. Luo SC, Chen JB, Chen CC and Chen YA collected and assembled the data. YY, Chang CH and P'eng FK performed the data analysis and interpretation. Wu CC and Chen JB contributed to the writing of the manuscript. All authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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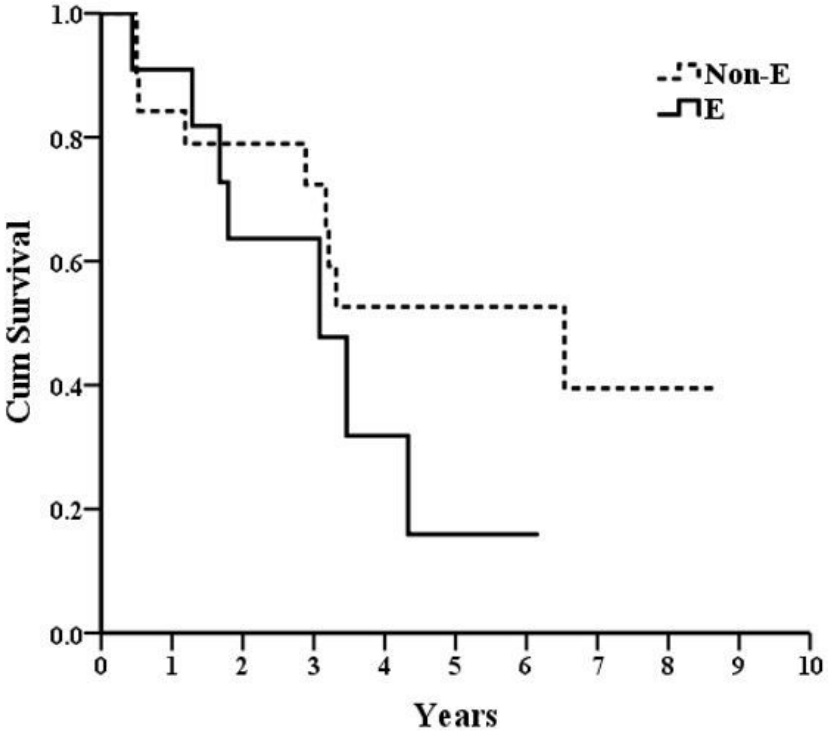
Figures



Group	0y	1y	2y	3y	4y	5y	6y	7y	8y
E	11	10	7	4	2	1	1	0	0
Non-E	19	16	14	11	6	5	5	3	2

Figure 1

Overall survival rate after colo- pancreaticoduodenectomy