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Colo-pancreaticoduodenectomy for Locally Advanced Colon Carcinoma- feasibility in patients manifesting as Acute Abdomen

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Abstract

Background

For locally advanced colon carcinoma that invades duodenum and/or pancreatic head is en-bloc right hemicolectomy plus pancreaticoduodenectomy (PD). This procedure may be also named as colo-pancreaticoduodenectomy (cPD). Patients with such carcinoma may abdomen. Emergent PD often leads to high postoperative morbidity and mortality. Here, we aimed to evaluate the feasibility and outcomes of emergent cPD, for patients with advanced colon carcinoma, manifest acute abdomen condition.

Patients and Methods

We retrospectively reviewed of 4,793 patients of colorectal cancer, receiving curative colectomy, during the period from 1993 and 2017. Among them, 30 had locally advanced right colon cancer and had received cPD. Among them, surgery of 11 patients was performed in emergent conditions (bowel obstruction 6, perforation 3, tumor bleeding 2). Selection criteria for emergent cPD were the following: (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 did not meet the above criteria received non-emergent cPD after a life-saving diverting ileostomy, followed by cPD, performed three months later. We analyzed these patients in terms of their clinicopathological characteristics, the early and long-term postoperative outcomes, and compared findings between emergent cPD group (e-group, n=11) and non-emergent cPD group (non-e group, n=19). After cPD, staged pancreaticojejunostomy was performed in all e-group, and on 15 of 19 patients in the non-e group.

Results

The non-e group was older, and had a higher incidence of associated comorbidities, while other clinicopathological characteristics were, similar between the two groups. 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

Emergent cPD is feasible in highly selected patients if performed by experienced surgeons. The early and long-term positive outcomes of emergent cPD are similar to those after non-emergent cPD in patients with acute abdominal conditions.

Introduction

The prevalence of colorectal carcinoma is increasing worldwide (1). In Taiwan, this cancer is ranked highest amongst new malignant cases, especially over the last two decades (2). The only promising cure at early stages is radical colectomy, performed for R0 resection (3). For locally advanced colorectal carcinoma, en-bloc is required for the involved adjacent organ (4). Multi-organ resectionS for colorectal carcinoma are often associated with higher postoperative morbidity and mortality (3-5).

When a right colon cancer directly infiltrates the duodenum near the ampulla of Vater or pancreatic head, the procedure of radical resection consists of a right hemicolectomy plus pancreaticoduodenectomy (PD)(5-25). We named such procedure as colo-pancreaticoduodenectomy (cPD).

The techniques of PD were demonstrated first by Kausch in Germany, and Whipple in the USA in the early 20th century. The complex procedure has remained basically unchanged for nearly a century. The PD procedure, also known as “Kausch-Whipple procedure” (26), is the standard for treating neoplasms or complex injuries or diseases involving duodenum and pancreatic head (26-34).
Recently, despite the lowering operative mortality of PD to <5 %, complication rates remain high (up to > 40 %)(26-34). The complexity of cPD, is greater than that of PD. In addition, cPD has more operative morbidities and mortalities (5-25). PD performed during emergency condition has further risks (20, 27-31, 33). Operative mortality of such emergent PD exceeds 20 to 40% (20, 27-31, 33). Patient’s preoperative conditions combined with PD etiology are important contributors to the surgical outcomes (29-31, 33).

Emergent resection of a bowel tumor is indicated for patients with acute abdomen caused by bowel obstruction, perforation or tumor bleeding (32). Our hospital is the only government-supported tertiary referral medical center in central Taiwan. It often admitted patients manifested life-threatening conditions of colorectal carcinoma. Few studies have yet reported on the emergent cPD for patients of locally advanced colorectal carcinoma presenting with serious acute abdominal conditions (30-32). To this end, we retrospectively reviewed patients to evaluate the feasibility of emergent cPD for patients with locally advanced colorectal carcinoma presenting with an acute abdomen.

Patients And Methods

Over a period of 25 years (from 1994 to 2018), we admitted 4,898 patients for radical curative resection to treat their colorectal carcinoma. Out of these patients, 30 had locally advanced colon carcinoma infiltrating duodenum and/or pancreatic head which needed a cPD. Of these 30 patients, 11 received cPD under emergent conditions (e-group). Their detailed information is shown in Table1. Causes of emergent cPD in this group were the following: 6, acute bowel obstruction; 2, tumor perforation following colonoscopic biopsy; one, spontaneous tumor perforation and 2, tumor bleeding.

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 period, a total of 742 PDs were performed in our hospital. Patients who received cPD not due to locally advanced colorectal carcinoma or for other diseases were excluded from our study. Those patients with locally advanced tumor to duodenal wall with well-preserved

ampullary area but no need for cPD (9), were also excluded. The choice of classical PD or pylorus preserving PD (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 two senior surgeons (CCW and FKP), while strategies of colon cancer resection were determined by another two colorectal surgeons (JBC and CCC), and two oncologist (CHC and YY) designed chemotherapies and target therapies.

Preoperative assessments for elective cPD: i.e., functional examinations of lung, heart, liver and kidney, were performed for all 19 patients in the non-e group. Their comorbidities were well controlled. The level of carcinoembryonic antigen was measured. Computed tomography (CT) or magnetic resonance imaging was also performed.

Selection criteria for emergent cPD patients with obstruction and perforation were as follows: [1] age £60 years, [2] body mass index <35 kg/m^2, [3] no poorly-controlled comorbidities in perforation cases, with estimated perforated duration £6 hours with no severe intra-abdominal contamination. For the other 19 patients (non-e group), after well-examined preoperative studies, their procedure of cPD was performed under an elective regular schedule.

The preoperative assessments for patients of locally advanced colon cancer presenting with an acute abdomen, were performed similarly for elective surgical treatments. These procedures were completed within two hours following admission to the emergency department. Emergent laparotomy was carried out to alleviate acute abdominal conditions, after fluid resuscitation and systemic antibiotic treatments. Diagnosis of invasion severity of colon cancer was typically made after exploratory laparotomy.

For two initially diagnosed perforation cases and one obstruction case, because general conditions of patients did not meet the criteria outlined above, received diverting ileostomy with omental patch to occlude perforation holes. Another older patient with tumor obstruction was treated first by diverting ileostomy. The procedure of cPD was then performed for these three patients three months later. They were categorized to the non-e group.

Pancreaticojejunostomy is the key procedure for reconstructing pancreatic remnant and the gastrointestinal tract. In 4 non-e group patients, the procedure involved the invagination method during the early periods of this study (prior to March 1996). Whereas for the later 15 patients in the non-e group, and all patients in the e-group, three months after cPD, we performed the staged pancreaticojejunostomy (30, 35, 36). Regarding the management of colon-related complications, colon leakage was treated with diverting ileostomy, intra-abdominal abscess was treated with percutaneous drainage (by surgeons JBC and CCC). Any complication or death occurring within 90 days after cPD were recorded as surgical complication or mortality. Complication severity was graded using the Dindo-Clavien classification (37). Definitions and severities of pancreatectomy-related complications followed those of the international study group of pancreatic surgery. These complications included postoperative pancreatic fistula (38), postpancreatectomy hemorrhage (39), delayed gastric empty (40) and bile leakage (41). These complications graded the severity of pancreatectomy-related morbidities. After patients had recovered from cPD, they were followed-up monthly at the outpatient clinic during the first following year, and thereafter at intervals of 3-6 months. On each visit, CT or magnetic resonance imaging was performed, and serum levels of carcinoembryonic antigen measured.

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

Resected specimens were sent to the pathology to determine the pathological characteristics and cancer stages of colorectal carcinoma. For cancer cell differentiation, the definition by the World Health Organization (42) was used. For cancer staging, we used the benchmark classification of the American Joint Committee for Cancer (8th edition)(42). The clinicopathological characteristics of patients, their early postoperative and long-term results after cPD were compared between the two groups.

Statistical Analysis

Continuous variables were presented as median (range), and compared using the Mann-Whitney U test. Frequencies were compared using Fisher's exact test or Pearson's χ^2 test as appropriate. Rates of overall survival (OS) up to July 2020 were calculated using Kaplan-Meier life table method, and compared across groups using log-Rank test. Differences with p values <0.05 were regarded as statistically significant.

Results

All cPD procedures were performed by open laparotomy.

Table 2 shows, clinicopathological characteristics of patients in both groups. Patient comorbidities in the non-e group 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, yet complication rates appeared high in both groups and with no inter-group differences (64% in e group vs. 42% in non-e group, 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 male patient in the non-e group had dehiscence of an invaginated pancreaticojejunostomy [grade C postoperative pancreatic fistula] with gastroduodenal artery stump bleeding [grade C postpancreatectomy hemorrhage]. Was rescued by an emergent total separation and closure of both pancreatic and intestinal stumps, peripancreatic irrigation and total parenteral nutrition (43, 45). Half a year later, he developed a chronic pancreatic fistula which was treated with fistulo-jejunostomy (44).

Although all procedures of cPD were grossly curative, pathological examination showed in three patients [1 in non-e group, 2 in e group] cancer exposure at the retroperitoneal dissection surface of the pancreatic head. They were categorized as R1 resection. These patients survived <2.5 years.

Figure 1 shows the OS rates of the two groups, and with no inter-group differences [p=0.192].

Discussion

We reviewed our 25-year experience on cPD for patients of locally advanced colon cancer. A nationwide survey in the Netherlands reported that the most common indication of cPD is first, locally advanced pancreatic head cancer (23) that directly invades colon or mesocolon, followed by locally invaded colon cancer at the duodenum and/or pancreatic head. The procedure of cPD, is rarely performed in gastrointestinal surgery. This is due to its complexity, difficulty and high risks. In certain acute situations, cPD is the efficacious path forward. According to surgeons at the Memorial Sloan Kettering Cancer Center, New York, the most complex surgical procedures in cancer surgery are esophagectomy, hepatectomy, pancreatectomy and total pelvic exenteration (45).

The above procedures, are recommended to be best performed at well-experienced medical centers. From our present study, we found similar postoperative courses in both cPD and PD. Therefore, a successful emergent cPD may be similarly done like a successful emergent PD. Emergent PD is associated with high postoperative morbidity and mortality, reaching 30% and 50% (30-33).

Gulle et al. (29) reported their operation on 10 patients with emergent PD to treat complex pancreaticoduodenal trauma with zero death. However, their complication rate is high (80%). All their patients were relatively young and healthy without challenging co-morbidities. Emergent

PD for non-trauma cases has risks higher than trauma cases, because of their often unrecognized preoperative poor conditions, and co-existed inflammation or organ dysfunction that lead to failed emergent PD (30, 31, 33).

Managing postoperative complications after emergent cPD is also an important issue after emergent PD. Performing cPD is itself a challenging, involving high levels of skills and long operation times. It requires meticulous and experienced care during the evaluation of perioperative period to minimize complications and deaths. Thus, the diagnosis and evaluation of preoperative general conditions of these patients should be well-surveyed to prevent occurrences of potential postoperative adverse events. Therefore, proper preoperative selection of patients is critical for the success of cPD. Despite high complication rates of emergent cPD in our patients, their rates of early and long term survivals rate appear acceptable.

Abdominal CT scan plays an important role in the preoperative diagnosis of such advanced cancer. However, in patients presented with acute abdomen, CT scan facilitates the visualization of tumors due to marked intestinal edema or marked intraperitoneal free air. When a right colon cancer is loosely adhered to the duodenal wall, it may be regarded as a duodenal invasion. Such cases were observed in our current study. Likewise, when a relatively small right colon cancer directly invades the pancreatic head, even with a small invaded area, the condition may be regarded as “no invasion”. Therefore, definite diagnosis of colon cancer with duodenum or pancreas invasion could be comfirmed only after “exploratory laparotomy”. Moreover, damage-controlled procedures can be given to those patients not fulfilling our criteria of emergent cPD.

Patients with advanced age, poorly controlled comorbidities, unstable vital signs, or obesity, are typically at risk of PD. They were therefore excluded from our emergent cPD when 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 destroy sutures in cPD early postoperative period. These patients are therefore not recommended for emergent cPD.

Acute massive bleeding from gastrointestinal malignancy is very rare but the sequel is grave. Once occurred, emergent resection to stop the bleeding is most likely the only life-saving option. The aforementioned patient selection criteria and managements for obstruction and perforation are not be applicable in bleeding cases. Trans-arterial embolization may be temporarily helpful for hemostasis (29, 46). However, due to abundant vascular collaterals in pancreaticoduodenal regions, total hemostasis is difficult. The resection of a bleeding tumor resection is still mandatory after embolic control of hemostasis.

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

Pancreaticojejunostomy has been considered as the “Achilles tendon” of PD. For a successful cPD, the management of the anastomosis is also crucial. During the early period of our study [before March, 1996], we had a case of grade C catastrophic pancreatic leakage with bleeding (disruption of pancreaticojejunostomy with massive internal bleeding). The patient fortunately survived after our timely and appropriate managements.

Intraoperative management for cPD adverse events, related or not related to techniques, is of great importance to reduce chances of operative mortality.

Staged pancreaticojejunostomy was routinely used for all PD after cases when the pancreatic duct size is small (<2mm), pancreatic parenchyma is soft or associated with large vessel resection or controlled troublesome comorbidity.

Staged pancreaticojejunostomy was firstly proposed by Japanese surgeons, Miyagawa and Makuuchi in 1994 (39). They covered the common hepatic each proper hepatic artery, and gastroduodenal artery stump using a sheet of pedicled greater omentum or liver falciform ligament (35, 36). A thin plastic tube was then inserted into the main pancreatic duct to totally exteriorize the pancreatic juice. Pancreatic juice was fed into intestine lumen through another tube jejunostomy, with the seromusculature sutured with the posterior wall of the pancreatic stump. The anastomosis was performed three months later by inserting the aforementioned plastic tube into the neighboring jejunal lumen.

The pedicled falciform ligament of the liver, or greater omentum is capable of covering the transected stump of gastroduodenal artery [the most common site of postpancreatectomy hemorrhage after PD](39). This vessel can be protected from erosion by the leaked out pancreatic juice. Actually, no catastrophic complication had occurred or even minor leakage occurred after staged pancreaticojejunostomy. This quarantined further the safety of cPD.

The experience of treating acute necrotizing pancreatitis is also helpful for treating pancreatic leakage after PD (46). An appropriate and timely management of complications after PD could improve healing and prevent operative death. The procedure of pancreatectomy for disruptured pancreatic anastomosis (28) has a high death rate (28, 40). It should therefore be avoided [43]. Even with the development of chronic pancreatic fistula, treatment by fistulojejunostomy can be effective without undesirable sequelae (44).

Delayed gastric empty is also a problematic adverse event of both PD and cPD. The event is likely related to the destruction of upper abdominal autonomic nerve plexus during the lymphadenectomy. The condition often requires prolonged hospitalization, long-term nasogastric decompression and total parenteral nutritional support. These management protocols could cause other systemic problems, like catheter sepsis, electrolyte imbalance, trace elements deficiencies, aspiration pneumonia and hepatic dysfunction. Some of these can be fatal. To avoid such severe complications, efforts to preserve the upper abdominal vagus nerve and sympathetic nerve plexus, could minimize delayed gastric emptying. Upper abdominal lymphadenectomy, which is typically carried out for periampullary or pancreatic cancer, is not mandatory for colon cancer patients.

Total removal of locally advanced colon cancer is essential to obtain a microscopic R0 resection. In our experience, R1 resection for colon cancer [cancer cells microscopically after operation] was actually palliative as no patient from the R1 resection had survived for more than 3 years.

The 5-years OS for locally advanced colorectal cancer is 51%. The reported 5-year OS rate after cPD for advanced colon cancer is 50 to 60% (26). Our non-e group patients showed prognosis comparable to the literatures (4-11). Because of the high incidence of lymph node metastasis, prognosis of the e-group patients is often poor. Nevertheless, both groups had similar OS. Histological TNM staging, lymph involvement and cancer cell differentiation are prognostic factors (5-12, 14, 15, 17-21, 23-25). The cancer conditions of our patients receiving cPD were similar to literatures on colon cancer patients. Development of new target agents or chemotherapeutic drugs is helpful to prolong survival.

Several limitations of the current study are as follows.

First, our comparison of two groups was not flawless. Because, patient selection or the choice of emergency procedure was based on perceived co-morbidities of patients, by the operating team, and that could be quite arbitrary. Nevertheless, no differences were found in other variables.

Second, the current study is a longitudinal observational cohort study. It was not a randomized-controlled trial because of the small sample size. Colon cancer that involves duodenum and /or pancreas is a distinctively unique presentation. During the 25-year duration of our study, diagnostic tools, surgical techniques, operative equipment, and peri-preoperative assessments have advanced markedly. Thus, our initial case-selection criteria in the e-group could 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 over the course of this study period (47). It is reasonable to assume that the safety range of emergent cPD could have also been extended.

Third, treatment strategies for locally advanced colon cancer were decided by our experienced colorectal and hepato-pancreatico-biliary surgeons as well as oncologists. Over the study period, some of the involved members of this research study had retired or shifted on to other projects. Although a senior surgeon (CCW) had led the treatment strategy of individual patients in a constant manner, there is an inherent discrepancy in the continuity of management for this complex disease. For example, the adjuvant therapies after elective or emergent cPD may have changed across different postoperative courses.

In the current study, we found no patients experiencing ileosolostomy leakage. Most postoperative complications were related to ileosotomy pancreatic or colon leakage, which could be managed by diverting proximal presence of ileostomy necrosis. Nevertheless, abscesses could be treated by percutaneous drainage. These complications should be diagnosed early and promptly treated.

Fourth, although staged pancreaticojejenectomy may improve safety of cPD of patients, additional admission and operations are needed for a complete pancreaticojejunostomy. Given new safe-guarded techniques on dealing with pancreatico anastomosis, the safety of cPD in single operation could be 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 colon cancer presenting acute abdomen. The long-term outcomes after emergent and non-emergent cPD are comparable.

Conclusions

Emergent cPD is feasible in highly selected groups when only performed by experienced colorectal and hepato-bilio-pancreatic surgeons. The early and long-term positive outcomes of emergent cPD are similar to those after non-emergent cPD in patients with life-threatening acute abdominal conditions.

Abbreviations

PD: pancreaticoduodenectomy; cPD:colo-pancreaticoduodenectomy; CT: Computed tomography; OS: overall survival.

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

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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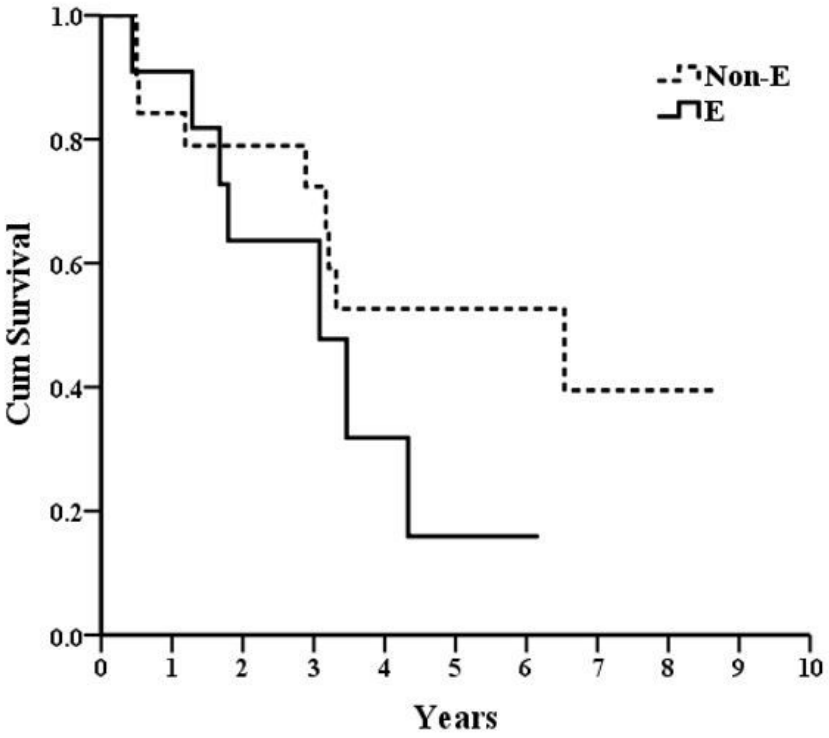
Figures



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