



ORIGINAL ARTICLE

Effects of antecolic versus retrocolic duodenojejunosomy on delayed gastric emptying after pyloric preserving pancreaticoduodenectomy in patients with periampullary tumors



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KEYWORDS

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Delayed gastric emptying

Summary *Background/Objective:* Delayed gastric emptying (DGE) is one of the most frequent complications after pyloric preserving pancreaticoduodenectomy (PPPD). The aim of this study is to evaluate the effect of antecolic versus retrocolic reconstruction of gastroenteric anastomosis on DGE after PPPD.

Methods: 30 patients with diagnosis of operable periampullary malignancies who candidate for PPPD, randomized in two equal groups. Gastroenteric reconstruction were done in two methods: antecolic and retrocolic. All data were collected by the same person who was completely blinded to the type of the procedure. Duration of the surgery, volume of bleeding and total volume of intraoperative blood product transfusion, time to nasogastric tube (NGT) removal, time to solid fluid toleration, volume of NGT secretions, need for NGT reinsertion, daily nausea after NGT extraction, fistula or leakage, gastric leakage, biliary leakage, postoperative abdominal or gastrointestinal bleeding requiring another operation, wound infection, intra-abdominal abscess, and any other systemic complications were measured and then analysed with SPSS software.

Results: According to the results, there was no significant differences between antecolic and retrocolic groups in terms of DGE ($p = 0.75$). Also, there were no significant differences

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between two groups in terms of duration of operation, volume of bleeding, blood product requirement, volume of NGT secretions, time to NGT removal, number of NGT re-insertion, time to tolerate solid foods, number of days of vomiting after NGT removal, total hospital stay. *Conclusion:* The route of gastroenteric (antecolic and retrocolic) reconstruction has no impact on DGE after PPPD.

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1. Introduction

Standard treatment of periampullary tumors is by different types of pancreaticoduodenectomy (PD) procedures and actually other treatment modalities such as chemo- or radiotherapy have no or modest effect on the fate of these patients.¹

Whipple surgery is the standard surgical procedure for these tumors for over 75 years but with several complications which results in the need for modification of these complicated operation that results in innovation of other types of this procedure such as pyloric preserving pancreaticoduodenectomy (PPPD) or different types of pancreatico-enteric anastomosis such as ductojejunostomy or pancreaticogastrostomy.² With advances in surgical techniques and multidisciplinary management of these cases, mortality of PD decreased from 30% to 5–6% in the last decade^{3,4} but its morbidity is still as high as 50%.^{5,6}

Delayed gastric emptying (DGE), bile leakage, pancreatic fistula, intra-abdominal abscesses, systemic infections, bleeding and ileus are among the most common complications of this procedure that still results in such high rate of morbidity after this operation.⁷ Because some authors report a higher rate of DGE after PPPD with different positions of duodenoenteric anastomosis, in this study, we compared incidence of DGE after antecolic versus retrocolic duodenojejunostomy after open PPPD in a small randomized clinical trial.

2. Material and methods

All 18–75-year-old patients with diagnosis of operable periampullary malignancies who were referred for surgery and were acceptable candidates for PPPD enrolled in this

study in Imam Reza Hospital, Tabriz University of medical sciences, Tabriz, Iran, from April 2016 to March 2017. Pre-operative biliary drainage by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD) were used in all patients with total serum bilirubin level over 10 mg/dl at least 2 weeks before the operation. *Table 1* shows the exclusion criteria that used for better selection of the patients.

2.1. Randomization and blinding

These patients were randomly assigned between two equal groups by Randlist[®] software: antecolic versus retrocolic reconstruction of duodenojejunostomy. The attending surgeon received a sealed envelope before proceeding to duodenoenteric anastomosis at the last step of the procedure. All perioperative clinical and para-clinical needed data were collected by the same person (Dr A.A.) during this period who was completely blinded to the type of the procedure which was done for the patient for complete 30 days period of follow-up.

2.2. Perioperative care and surgical technique

We followed all the rules for standard care of icteric patient before and after the surgery. All patients were fully hydrated and took prophylactic antibiotics. In the operative room nasogastric (NG) tube and Foley catheter and central venous pressure (CVP) monitoring and arterial lines were inserted and general anaesthesia were used for all patients with the same standard techniques of our hospital.

Our center has no experience with laparoscopic PD and all the procedures was in an open technique. Surgical approach started by upper midline or Chevron incision according to surgeon's choice and all the surgeries is done by

Table 1 Exclusion criteria.

Exclusion Criteria

- Aged over 75 or 18 years old
- Previous upper abdominal surgery
- Preoperative signs of inoperability according to imaging studies (e.g., mesenteric or portal vein or superior mesenteric artery involvement, distant metastases, nearby organ involvement)
- Preservation of pylorus is not feasible or contraindicated
- General conditions not suitable for a Whipple procedure (e.g., heart or renal failure) were excluded from the study.
- Liver cirrhosis
- Inoperable according to intraoperative findings
- Death during the operation.

the staff surgeons (Dr. F.K. and Dr. MB.F.). For prevention of infection 1 g of intravenous cefazolin and for DVT prophylaxis, 5000 IU of subcutaneous unfractionated heparin was injected just before the incision and the laparotomy incision was covered by sterile plastic wound retractor-protectors. For all patients after completion of resection of pancreas head, duodenum, gallbladder and regional lymphadenectomy, reconstruction was done by preservation of the pylorus in this manner:

1. Pancreaticojejunostomy in two layers: first a posterior layer of end-to-side invagination by 3-0 polydioxanone (PDS[®], Ethicon, Johnson & Johnson) and then ductojejunostomy by microsurgical technique and magnification by 4-0, 5-0 or 6-0 PDS[®] according to the size of the duct and then completion of anterior layer of invagination with another layer of 3-0 PDS[®]
2. Choleducojejunostomy on 5–7 cm distal to the first anastomosis with 3-0 or 4-0 PDS[®] according to the size of the duct in an end to side fashion in one layer.
3. Duodenojejunostomy 2 cm distal to pylorus in an end to side fashion in 2 layers by 2-0 or 3-0 PDS[®], 5–10 cm after the previous anastomosis in retrocolic position or 20–30 cm distal to previous site of Treitz ligament in antecolic position based on randomization number that included in the sealed pocket that opened at this time.

At the end of the operation and completion of haemostasis, 2 corrugate open drains were inserted in sub-hepatic and peri-pancreatic area and abdominal wall closed in anatomical layers. All patients were transferred to intensive care unit (ICU) or specialized surgical ward according to their postoperative condition and received prophylactic subcutaneous unfractionated heparin and compression stockings till they can be fully mobilized. Intravenous crystalloids, antibiotics (cefazolin and metronidazole) and pantoprazole (40 mg twice a day) were infused for 5 days and subcutaneous octreotide continued for 48–72 h after the operation in high risk pancreatic anastomosis (patient with very small ducts or fragile pancreas tissue). Blood product transfusions were decided according to perioperative lab data or surgeon or anaesthesiologist's decision in emergency situations. The antibiotic regimen was stopped after 48 h and continued or changed according to the results of any cultures or any signs of other infections. NG tube were removed after 48 h if no bleeding was seen and when its excretion was less than 50 millilitre (ml) per 6 h. If the patients' condition was good and gas passing is normal, sips of water was started in day 4 and after that normal liquid or solid diet was started in advance and abdominal drains were removed after 5th day if their drainage was less than 50 ml per day. The patient was discharged if the course of the hospital stay is uneventful and when all the drains were removed and patient tolerated solid food and no signs of infection or leakage or any other complications were detected.

2.3. Patient characteristics and definitions

The following data were collected for each patient using a checklist: age, sex, body mass index, interval between the

initiation of symptoms and doing surgery (months), type of the disease (duodenal mucosal, distal bile duct or pancreas tumor). Also, we collected any data about other postoperative complications including pancreatic fistula or leakage, gastric leakage, biliary leakage, postoperative abdominal or gastrointestinal bleeding requiring another operation, wound infection, intraabdominal abscess, and any other systemic complications (pulmonary, cardiac, renal, ...) and deep vein thrombosis (DVT). Patients were followed for 1 month after the operation or until in-hospital death. We use definitions accepted by International Study Group of Pancreatic Surgery (ISGPS) for post-pancreatectomy complications including DGE.¹³ If there is no other signs of anastomosis leakage or other metabolic or intraabdominal causes of ileus, then DGE were defined as: grade A (NGT for 4–7 days or reinserted after 3rd day, inability to tolerate food after 7th day), grade B (NGT for 8–14 days or reinserted after 7th day, inability to tolerate food after 14th day) or grade C (need for NGT for more than 14 days or reinserted after day 14, inability to tolerate food after 21 day).¹⁴ We followed this definition for our patients and didn't use scintigraphy or other imaging studies for definite diagnosis, but when other complications were suspected due to clinical course of the patient, we proceeded to abdominal ultrasonography or computed tomography (CT) scan to rule out other complications such as pancreatic fistula or intra-abdominal abscesses and managed the patient according to the final diagnosis.

2.4. Ethics

The study was designed by Surgery group and approved by the Institutional Review Board and Ethics Committee of Tabriz University of Medical Sciences as a prospective randomized clinical trial. All patients informed about the design and aims of this study and signed the consent letter. Costs of study provided by Vice Chancellor for Research (VCR) of Tabriz University of Medical Sciences.

2.5. Statistical analysing

All data analysed with SPSS version of 16. We used statistically descriptive method. Qualitative data analysed by K-2 (χ^2) or Fisher Exact Test. Quantitative data were compared between two groups by independent-sample's t-test. P-Value which was lesser than 0.05 considered as reliable. For assessment of normal distribution of data, Kolmogorov–Smirnov test was used. RR-Indexes with only 95% confidence interval reported. For neutralizing the effect of conflicted variables multi-variable regression models was used.

3. Results

Sixty-seven patients were referred to our center with periampullary tumors during this period but 45 of them was found operable during the procedure and PPPD are amenable in 30 of them. At the end of the study the remaining 30 patients were treated due to randomization number between two equal group who have either antecolic or retrocolic duodenoenteric anastomosis after

Table 2 Cause of the disease and its pathologic stage according to American Joint Committee for Cancer (AJCC) staging system, 8th edition^a.

	Antecolic group (n = 15)	Retrocolic group (n = 15)
Pathologic cause		
Pancreas	8	10
Duodenal mucosa	2	2
Distal common bile duct	4	2
Undefinable	1	1
Pathologic staging		
Stage Ia	1	0
Stage Ib	1	1
Stage IIa	1	3
Stage IIb	5	5
Stage IIIa	5	4
Stage IIIb	1	2

^a Gonzalez, R.S. TNM staging. [PathologyOutlines.com](http://www.pathologyoutlines.com/topic/ampullatnmamp.html) website. <http://www.pathologyoutlines.com/topic/ampullatnmamp.html>.

completion of PPPD. Table 2 shows the cause of the disease and pathologic stage of the disease in each group. Statistically, there was no significant difference between the two groups in the following items: sex and age, body mass index, duration of operation, volume of bleeding, blood product requirement, volume of NGT secretions in first 48 h after the surgery, time to NGT removal, time to tolerate solid foods, number of days of vomiting after NGT removal, total hospital stay (Table 3). One patient was died in each group: one due to pancreatic anastomosis leakage in retrocolic group in postoperative day (POD) 25, and the other one due to sudden death probable pulmonary embolism in POD 3 in antecolic group (patient's family regretted to do an autopsy for definite diagnosis). We have one temporary biliary leakage in retrocolic group which was stopped spontaneously in POD 5. We have no major skin or other

intraabdominal or systemic infections (except for the patient who was died due to pancreatic anastomosis leakage). Grade A DGE was found in 2 (13.3%) patients in antecolic and 3 (20%) patients in retrocolic group. We have no other grades of DGE in our patients. Mean total hospital stay was 7.7 (7–12 days).

4. Discussion

Standard one stage Whipple pancreaticoduodenectomy (PD) or pylorus preserving pancreaticoduodenectomy (PPPD) are now the accepted standard surgery for all resectable peri-ampullary tumors but while the mortality of this procedures reduced during the last decades, their morbidity is still very high and need for research in the modification of the techniques required emergently. One of important complications after PD or PPPD is Delayed Gastric Emptying (DGE) with incidence of 14–61% (maximum prevalence of 81%) and actually is a rule after this operation but with different severities.^{8–10} International Study Group of Pancreatic Surgery (ISGPS) defined the DGE as gastro-paresis with prolonged drainage from naso-orogastric tube and food intolerance for more than one week after the operation. Patients may need enteral or parenteral nutrition if they can't tolerate this period of fasting and sometimes they require surgical intervention.^{11,12}

Many factors have been suggested as the cause of DGE: type of the procedure (pyloric preservation, subtotal stomach preserving or distal gastrectomy), open versus laparoscopic surgery, volume of center experience with PD, route of gastro-enteric reconstruction (antecolic or retrocolic),^{13,14} preservation of the right gastric artery, gastric/duodenal devascularization, length of the preserved proximal portion of the duodenum, pylorus preservation, type of pancreatic anastomosis (pancreaticogastrostomy or pancreaticojejunostomy), volume of preoperative gastric juice, duration of gastric tube placement, administration of prokinetic agents, diabetic gastroparesis, history of

Table 3 Operative data and post-operative complications.

	Antecolic group	Retrocolic group	P-Value
Age (years)	53.6 ± 9.76 (31–70)	52.93 ± 8.76(33–62)	0.84
Gender	Male: 9 (60%) Female: 6 (40%)	Male: 10 (66.6%) Female: 5 (33.3%)	0.48
Mean total hospital stay (days)	8.93 (7–12)	8.86 (7–12)	0.82
Mean number of packed cell needed during surgery	1.334	1.067	0.76
Mean number of fresh frozen plasma needed during surgery	0.601	0.601	1
Mean of duration of surgery (hours)	4.5 ± 0.59	4.66 ± 0.77	0.166
Volume of bleeding during surgery (ml)	466.66 ± 147.19	476.16 ± 66.51	0.75
Time of NG-Tube using (days)	3.28 ± 0.91 (2 to 5)	3.64 ± 1.15 (3 to 6)	0.58
Period until solid fluid toleration (days)	7.85 ± 1.16 (7 to 11)	8.5 ± 1.6 (7 to 12)	0.182
Mean of NG-Tube secretion volume for 48 h after surgery (ml)	137.14 ± 45.98 (60 to 200)	179.28 ± 53.84 (100 to 250)	0.58
Delayed Gastric Emptying (DGE)	2 patients 13.3%	3 patients 20%	0.75

cardiovascular or renal disease, type of the tumor, preoperative biliary drainage, perioperative general condition of the patients (for example mechanical ventilation in ICU). In addition, other intra-abdominal complications such as pancreatic fistula or leak, biliary fistula, pancreatitis, pancreatic fibrosis, intra-abdominal collections or abscesses or bleeding mentioned as factors that can accompany or induce DGE.^{10,14–17}

Some studies mentioned the “pylorus preservation” as one the most important factors that might negatively influence the rate of DGE after PD,^{7,12} probably due to denervation or devascularization of pylorus, but this is controversial and a meticulous dissection around the pylorus may theoretically decrease this complication. As our study shows the rate of this complication after PPPD in our patients is only 16% and all of the cases were mild and treated only by waiting without any need for further intervention. Some authors suggested that resection of the pylorus and preservation of 95% of the stomach (subtotal stomach preserving PD or SSPPD) may theoretically reduce this complication by removing a denervated or devascularized pylorus, but in my opinion because of a large number of acid secreting cells in the antrum of the stomach, this type of procedure may highly increase the rate of postoperative marginal ulcers in the site of gastrojejunostomy. A large and comprehensive meta-analysis of 650 patients couldn't confirm any improvement in the results of the surgery comparing SSPPD with PPPD, but showed slight decrease in the rate of DGE after this procedure.¹²

Method of gastro-enteric anastomosis is another important factor that may influence incidence of DGE. Some studies showed antecolic reconstruction significantly decreased the DGE^{13,14,18} because it may decrease the risk of mechanical problems by better fixation of stomach that prevent angulation or torsion.¹⁹ Other studies showed no significant difference between these two approaches.^{20,21} In my opinion retrocolic reconstruction is more anatomic and the position of the duodenoenteric anastomosis is more similar to the normal anatomic retrocolic position of gastroduodenal system. In obese patients with a bulky omentum or with a bulky transverse colon with a high content of fat in the transverse mesocolon, antecolic reconstruction of duodenoenteric anastomosis may not be easily feasible and may be associated with a higher tension on anastomosis and increases the risk of leakage or DGE.

Nojiri et al, have better discussed radiologically and mathematically about this very important feature of this procedure.²² Their multivariate analysis shows that “*a sagittal fundus anastomotic angle > 60 degrees was the only independent risk factor of delayed gastric emptying*”. Their discussion about these angles are very sophisticated and following their rules is very difficult in practice and may slightly increase the time of the procedure.

Parmar et al, researched about factors that influence DGE after PD. They revealed factors during the operation such as pylorus preservation, insertion of drainage tube and method of gastrojejunostomy reconstruction (antecolic or retrocolic) not affect the incidence of DGE.²³ Eshuis et al, also showed there is no significant relation between method of gastro-enteric reconstruction and DGE, although

primary DGE (without intra-abdominal complications) in retrocolic group was higher.^{6–9} This is just the same of our study which shows that the rate of DGE is slightly more prevalent in retrocolic group (20% Vs 13%) but this difference is not statistically significant. Unfortunately our study was done in a very small group and has not enough power to compare rate of this complication and we should do this study in a larger group of patients.

In another study, Gangavatiker et al confirm these result but they recommended older age can be a risk factor for DGE.²⁰ Imamura et al, recommended vertical retrocolic duodenojejunostomy as an acceptable procedure for decreasing the rate of DGE and may cause to better weight gain by moderate gastric emptying. Although incidence of DGE in antecolic group was lower but statistically is not significant. In their study, nutritional status and gastric emptying variables assessed by the C-acetate breath test for one year after operation.¹⁹

In Summary, DGE is a painful state for patients which significantly affects the patient's quality of life and results in the patients and also surgeon's discomfort, and prolonged hospital stay and increasing the total costs. Higher grades of DGE may increase the rate of other complications such as hospital acquired infections, GI bleeding, anastomotic leakage, pancreatic fistula, multi-organ failure and death.¹² Treatment of DGE in mild cases is usually straightforward and waiting is all thing that is required but in severe cases, we should start a root of feeding such as total parenteral nutrition or feeding jejunostomy specially for cachectic patients which significantly increase the disease's morbidity and mortality. This means that the best treatment of this complication is prevention but the causes of this complex complication is not completely defined and further investigation is needed in the future.

5. Conclusion

The route of duodenoenteric (antecolic and retrocolic) reconstruction has no statistically significant impact on DGE after PPPD.

Conflict of interest

None.

Patient consent

Written informed consents were obtained from all patients. A copy of the written consents is available for review by the Editor-in-Chief of this journal on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.asjsur.2019.01.007>.

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