



# Delayed gastric emptying is associated with pylorus-preserving but not classical Whipple pancreaticoduodenectomy: A review of the literature and critical reappraisal of the implicated pathomechanism

Kosmas I Paraskevas, Costas Avgerinos, Costas Manes, Dimitris Lytras, Christos Dervenis

Kosmas I Paraskevas, 2<sup>nd</sup> Departments of Surgery, Agia Olga General Hospital, Athens, Greece

Costas Avgerinos, Costas Manes, Dimitris Lytras, Christos Dervenis, 1<sup>st</sup> Departments of Surgery, Agia Olga General Hospital, Athens, Greece

Correspondence to: Christos Dervenis, MD, Head of the Department, Unit of Liver Surgery, 1<sup>st</sup> Department of Surgery, Agia Olga Hospital, 3-5 Agias Olgas Str, Nea Ionia 14233, Greece. [chrisder@otenet.gr](mailto:chrisder@otenet.gr)

Fax: +30-210-2793969

Received: 2006-05-31 Accepted: 2006-06-25

serving but not classical Whipple pancreaticoduodenectomy: A review of the literature and critical reappraisal of the implicated pathomechanism. *World J Gastroenterol* 2006; 12(37): 5951-5958

<http://www.wjgnet.com/1007-9327/12/5951.asp>

## Abstract

Pylorus-preserving pancreaticoduodenectomy (PPPD) is nowadays considered the treatment of choice for periampullary tumors, namely carcinoma of the head, neck, or uncinate process of the pancreas, the ampulla of Vater, distal common bile duct or carcinoma of the peri-Vaterian duodenum. Delayed gastric emptying (DGE) comprises one of the most troublesome complications of this procedure. A search of the literature using Pubmed/Medline was performed to identify clinical trials examining the incidence rate of DGE following standard Whipple pancreaticoduodenectomy (PD) vs PPPD. Additionally we performed a thorough in-depth analysis of the implicated pathomechanism underlying the occurrence of DGE after PPPD. In contrast to early studies, the majority of recently performed clinical trials demonstrated no significant association between the occurrence of DGE with either PD or PPPD. PD and PPPD procedures are equally effective operations regarding the postoperative occurrence of DGE. Further randomized trials are required to investigate the efficacy of a recently reported (but not yet tested in large-scale studies) modification, that is, PPPD with antecolic duodenojejunostomy.

© 2006 The WJG Press. All rights reserved.

**Key words:** Pylorus-preserving pancreaticoduodenectomy; Whipple pancreaticoduodenectomy; Delayed gastric emptying; Pancreatic surgery

Paraskevas KI, Avgerinos C, Manes C, Lytras D, Dervenis C. Delayed gastric emptying is associated with pylorus-pre-

## INTRODUCTION

The introduction of partial pancreaticoduodenectomy for the treatment of carcinoma of the ampulla of Vater dates back to almost a century ago and is credited to Kausch, a German surgeon from Berlin<sup>[1]</sup>. Then, in 1935 Whipple and associates redefined this procedure as a two-stage pancreaticoduodenectomy, where the pylorus and proximal duodenum are closed and preserved, while gastrointestinal continuity is re-established via a gastrojejunostomy<sup>[2]</sup>. Six years later, the first successful one-stage radical pancreaticoduodenectomy in which the distal stomach, pylorus and duodenum are removed, was reported independently by Whipple<sup>[3]</sup> and Trimble and coworkers<sup>[4]</sup>. Whipple is credited with popularizing the procedure, which now bears his name. Whipple pancreaticoduodenectomy (PD) has become the standard procedure of choice for many decades for the treatment of benign disorders requiring pancreaticoduodenectomy (such as chronic pancreatitis)<sup>[5]</sup>, as well as for the treatment of periampullary tumors (carcinoma of the head, neck, or uncinate process of the pancreas, ampulla of the Vater, distal common bile duct, or peri-Vaterian duodenum)<sup>[6,7]</sup>. In 1978, Traverso and Longmire<sup>[8]</sup> reported a technique by which the whole stomach and 2.5 cm of the duodenum are preserved, restoring the gastrointestinal continuity by duodenojejunostomy. By application of pylorus-preserving pancreaticoduodenectomy (PPPD), the postgastrectomy syndrome (postprandial dumping, diarrhea, dyspepsia, nausea and vomiting) following Whipple resection is reduced and better functional results are achieved<sup>[9]</sup>. Although this technique has been initially reported by Watson<sup>[10]</sup> more than three decades before, the study by Traverso and Longmire<sup>[8]</sup> did not receive enough attention and has not been widely applied. In recent years, PPPD has been used increasingly by many surgeons, and is

considered the treatment of choice in many pancreatic surgery reference centers worldwide, despite the opinion that PPPD does not allow adequate resection of pancreatic or periampullary tumors<sup>[11,12]</sup>.

A shorter operating time and a reduced intraoperative blood loss as a result of omission of gastric resection requiring the transfusion of fewer units of blood, as well as avoidance of PD-related dumping syndrome, better postoperative weight gain and a better quality of life, are considered advantages of PPPD over PD<sup>[8,13-20]</sup>. However, PPPD has been linked with a major drawback, that is, delayed gastric emptying (DGE), which is responsible for prolonged hospital stay and increased associated morbidity<sup>[11,21-23]</sup>. DGE has been reported in early studies to occur in up to 70% of patients undergoing PPPD procedure<sup>[11,14,15,22-28]</sup>. Although the incidence of DGE appears to be declining in later published reports<sup>[5,29-31]</sup>, DGE remains a leading cause of PPPD postoperative complications. The concern regarding an increased incidence of DGE following PPPD has prevented the adoption of this technique by some major American pancreatic centers<sup>[32]</sup>.

Due to the fact that no uniform definition for DGE following pancreatic surgery exists, numerous controversial opinions have been reported regarding the efficacy of these techniques as causative factors for postoperative DGE occurrence. In an attempt to demonstrate which procedure, PD or PPPD, is preferable with regards to post-operative DGE occurrence, we performed a review of randomized, controlled trials in the English literature investigating the incidence of DGE following PPPD compared with PD. We further analyzed the various implicated pathomechanisms leading to the occurrence of DGE.

## DEFINITION OF DGE

The occurrence of DGE following PPPD is initially reported by Warsaw and Torchiana<sup>[22]</sup>. In their study that included 8 patients undergoing PPPD, only 1 tolerated solid food within 10 postoperative days. Early studies have used a wide variety of definitions for DGE following pancreatic surgery. Some researchers have defined DGE as the inability to tolerate a regular or normal diet by the tenth<sup>[14,22,27]</sup> or fourteenth<sup>[26]</sup> postoperative day, or the start of a liquid diet after  $\geq 7$  d<sup>[25]</sup>. Others have described DGE as gastric stasis requiring gastric suction for 7 d<sup>[11,15]</sup> or  $\geq 10$  d<sup>[24,28]</sup>.

In the recent years, although various definitions for DGE exist, 3 seem to be most widely acceptable. (1) According to the first definition<sup>[24]</sup>, DGE occurs when the nasogastric tube is left in place for  $\geq 10$  d plus one of the following: emesis after removal of the nasogastric tube, reinsertion of a nasogastric tube, postoperative use of prokinetic agents after the 10<sup>th</sup> postoperative day, or failure to progress with diet. (2) According to the second definition<sup>[33]</sup>, DGE occurs when nasogastric intubation is required  $\geq 10$  d following the operation, or is reinserted due to vomiting. (3) According to the third definition<sup>[34]</sup>, DGE occurs when nasogastric intubation is required  $\geq 10$  d following the procedure or when a solid diet cannot be tolerated on or before the 14<sup>th</sup> postoperative day.

Independent of the correct definition, DGE not only leads to repeated episodes of nausea and vomiting, but also has an impact on postoperative weight gain, duration of hospitalization<sup>[26]</sup> and related morbidity, while it may also lead to fatal aspiration and pneumonia<sup>[35]</sup>. It is therefore a dangerous and potentially life-threatening complication.

## WHAT IS THE PATHOMECHANISM UNDERLYING THE OCCURRENCE OF DGE?

A number of theories have been postulated to explain the occurrence of DGE after PPPD. Physiological gastric emptying and motility of the digestive system are complex processes that are controlled and regulated by complicated physiological mechanisms. Tonic contractions of the proximal stomach are important for the transfer of liquid food from the stomach to the duodenum<sup>[36,37]</sup>, while peristaltic contractions of the distal stomach are of primary importance for reducing the size of the solid food particles and for the transfer of solid food to the duodenum<sup>[38]</sup>. Furthermore, certain properties of ingested food, such as volume, osmolality, pH and nutrient content, may down-regulate the motility of the digestive system, either via vagal and splanchnic sensory pathways which mediate inhibition of gastric motility induced by duodenal distension<sup>[39]</sup>, or *via* cholecystokin- and secretin-mediated pathways<sup>[40]</sup>.

Cholecystokinin (CKK) has been shown in animals and humans to inhibit gastric emptying (especially the liquid-phase emptying of the stomach)<sup>[41]</sup> *via* a vagal capsaicin-sensitive afferent pathway and by stimulating phasic and tonic pyloric motility<sup>[42-45]</sup>. Muller and associates<sup>[46]</sup> reported that CCK levels decrease from  $1.1 \pm 0.2$  pmol/L preoperatively to  $0.8 \pm 0.2$  pmol/L 10 d postoperatively, and to  $0.5 \pm 0.1$  pmol/L following PPPD, though no statistical significance could be demonstrated. The decrease in CCK levels is attributed to the resection of the duodenum, because high concentrations of CCK are found in the duodenal mucosa.

An alternative explanation is that the reduction of CCK levels is an adaptive response to DGE. Large amounts of CCK can also be released from the jejunum, as proven by the fact that bypassing of the duodenum in patients with Billroth II gastrectomy does not decrease CCK secretion after ingestion of fats<sup>[47]</sup>. A finding that supports this theory is that blockage of CCK receptors with antagonists accelerates gastric emptying<sup>[48]</sup>.

The role of plasma secretin levels in the development of DGE following PPPD remains controversial and has not yet been fully elucidated<sup>[46,49-50]</sup>. Another mechanism that has been demonstrated to influence food transit is CCK-mediated pancreatic polypeptide (PP) release, which is mainly controlled by vagal cholinergic mechanisms<sup>[51-53]</sup>. Studies in dogs and humans have shown that the duodenum and vagal innervation are necessary for normal postprandial release of PP from pancreas<sup>[54,55]</sup>. PPPD has been shown to be significantly associated with reduction of PP levels compared with the preoperative findings<sup>[46]</sup>. This reduction seems to be due to resection of the pancreatic head, where the majority of PP-producing cells

are located<sup>[54]</sup>.

Other researchers support the theory that DGE occurs as a direct result of the removal of the duodenum, which influences gastric secretion and emptying as well as pancreatic and biliary secretion, thus playing an important role in the regulation of pancreatic hormone release<sup>[56,57]</sup>. In addition, duodenectomy disrupts the coordination of gastric and intestinal migrating motor complexes<sup>[58]</sup>, decreases the postprandial PP release<sup>[59]</sup>, and abolishes the interdigestive cycles of plasma PP<sup>[54]</sup>. Other investigators believe that preservation of the duodenal pacemaker located 0.5-1 cm distally from the pylorus should be the mainstay of the procedure, in order to avoid disturbances in normal gastric peristalsis<sup>[60]</sup>. Gastric dysrhythmias probably exacerbated by some intra-abdominal complications such as an anastomotic leak or an abscess have also been thought to be the causative factor for DGE following PPPD<sup>[61]</sup>. In addition, problems caused by the surgical procedure itself, namely the injury to the nerve of Latarjet, or placement of suture material through the pyloric muscle resulting in ischemia of the gastroduodenal segments and gastroparesis, have similarly been implicated<sup>[15]</sup>.

Multiple other causative agents have been implicated as etiological factors for DGE after PPPD, namely intra-abdominal complications, such as a leakage or an abscess<sup>[16,26,61,62]</sup>, postoperative pancreatitis<sup>[63]</sup>, pancreatic fibrosis<sup>[64]</sup>, preoperative cholangitis<sup>[62]</sup>, pylorospasm secondary to vagal injuries that requires the performance of pyloromyotomy<sup>[65]</sup>, alternation of the endocrinologic milieu<sup>[15,19]</sup>, early enteral nutrition commencing on the first postoperative day<sup>[66]</sup>, and torsion or angulation of the reconstructed alimentary tract<sup>[23,67]</sup>. It has been advocated that preservation of the right gastric artery is essential for avoidance of DGE, because of its arterial supply to the pylorus and antrum<sup>[23]</sup>, although there are other investigators who do not support this theory<sup>[64]</sup>. A more recent experimental study suggests that division of neurovascular supply to the pylorus and/or transection of the duodenum may lead to DGE following PPPD<sup>[68]</sup>. These investigators underlined that, besides the right gastric artery, additional preservation of the supraduodenal artery, as well as conservation of the pyloric branch of the vagus nerve, are crucial for avoidance of DGE following PPPD.

In an interesting study from two surgical institutes in the Netherlands<sup>[69]</sup>, the choice of Billroth I (proximal end-to-end duodenojejunostomy) or Billroth II (end-to-side pancreatojejunostomy at the end of the jejunal loop, followed by end-to-side hepaticojejunostomy and an end-to-side duodenojejunostomy) type of reconstruction has been shown to influence DGE after PPPD. Although significantly less procedure-related complications were noted following Billroth I compared to Billroth II type of reconstruction (18% *vs* 42% respectively,  $P < 0.05$ ), DGE occurred in significantly more patients receiving Billroth I compared to Billroth II type of reconstruction (76% *vs* 32% respectively,  $P < 0.05$ ).

The type of reconstruction of pancreaticogastrointestinal continuity following pancreatoduodenectomy has also been implicated to play a significant role in the

development of DGE. A randomized study comparing pancreaticogastrostomy [PG] (69 patients) *vs* end-to-side pancreatojejunostomy [PJ] (82 patients)<sup>[70]</sup>, showed that PG is superior regarding DGE rates (2 *vs* 10 patients, or 3% *vs* 12%, respectively,  $P = 0.03$ ). By using the PG reconstructive technique (a single layer of nonabsorbable interrupted stitches on the posterior wall of the stomach)<sup>[71]</sup> instead of PJ (single layer pancreatojejunal or duct to mucosa technique)<sup>[72]</sup>, the authors found that significantly less complications occur (25% *vs* 68%, respectively,  $P = 0.002$ ). More specifically, the lower rates of biliary fistulae (0% *vs* 8.5%, respectively,  $P = 0.01$ ) and intra-abdominal fluid collections (10% *vs* 27%, respectively,  $P = 0.01$ ) following PG compared with PJ, are the main culprits for the decreased rates of DGE.

Postoperative complications have been reported to correlate significantly with the occurrence of DGE in other trials as well. Horstmann and associates<sup>[73]</sup> showed that the incidence of DGE increases from 1% when no postoperative complications occur, to 28% and 43% respectively when moderate (wound infection, temporary cardiopulmonary complications, transient occurrence of amylase/lipase-rich drainage fluid without signs of sepsis) and severe (anastomotic leakage, bleeding, septic complications, reoperation) complications occur ( $P < 0.0001$ ). The results of several other studies lend support to this theory<sup>[16,27,33,74-77]</sup>.

An in-depth analysis of the physiology of the mechanism underlying the occurrence of DGE has also been reported, showing that the initiation of interdigestive phase III is closely related to the elevation of plasma motilin concentration<sup>[78]</sup>. Motilin, a 22-aminoacid residue polypeptide, originates in motilin cells, which are scattered in the duodenal epithelium<sup>[78]</sup>. Erythromycin and related 14-member macrolide compounds act as motilin agonists by binding to motilin receptors, which are largely confined to the antrum of the stomach and the upper duodenum<sup>[79]</sup>, thus initiating phase 3 activity of the interdigestive migratory motor complex (MMC)<sup>[80-81]</sup>. An early study<sup>[24]</sup> showed that patients administering high doses (200 mg) of erythromycin every 6 h from postoperative d 3 to 10 have a 53% reduction in the incidence of DGE compared with placebo.

Studies in unfed normal patients have shown that high doses of erythromycin (200-300 mg) induce strong, prolonged bursts of antral contraction, which are not propagated to the small intestine<sup>[82,83]</sup>. On the contrary, erythromycin administered in low doses (40 mg) induces premature phase 3, commencing in the stomach and migrating through the small intestine, which is similar to spontaneously occurring phase 3<sup>[82]</sup>. To test this hypothesis, Ohwada and coworkers<sup>[84]</sup> performed a prospective randomized, placebo-controlled trial investigating the effect of low-dose erythromycin *vs* placebo administration on DGE following PPPD and demonstrated that intravenous administration of erythromycin lactobionate (1 mg/kg) in 50 mL of 0.9% saline, given over 15 min through a central venous route every 8 h from postoperative d 1 to 14 results in reduction in the incidence of DGE following PPPD compared with placebo (14.3% *vs* 57.1% for erythromycin and placebo respectively,  $P = 0.04$ ). Use of low-dose

erythromycin is significantly associated with induction of phase 3 of the MMC and initiation of phase 3-like contractions ( $P < 0.0001$ ), earlier nasogastric tube removal ( $P < 0.001$ ) and earlier progression to diet ( $P < 0.003$ ). In contrast, the number of patients who had a nasogastric tube reinserted and emesis after nasogastric tube removal was similar in both groups. Still, erythromycin administration was associated with a 75% reduction in the incidence of DGE. In addition, a stepwise multiple regression analysis using a Cox proportional hazard model, showed that erythromycin and preservation of right gastric artery are significant covariates. Right gastric artery removal is a predictive factor for the effectiveness of erythromycin. The authors concluded that a low dose of erythromycin is not only more effective in reducing DGE after PPPD, but is also associated with a much lower rate of adverse effects compared with a high dose.

Octreotide, a long-lasting somatostatin analogue<sup>[85]</sup>, administered preoperatively and continued postoperatively for 7 d at a dosage of 100 µg given subcutaneously 3 times a day has been reported to accelerate the rate of gastric emptying<sup>[86]</sup>. A randomized, placebo controlled trial in healthy volunteers<sup>[87]</sup>, showed that administration of octreotide in the above-mentioned dosage can significantly accelerate gastric emptying compared to placebo ( $P < 0.05$ ). It is hypothesized that this occurs as a result of the suppression of postprandial CCK release. A role in the prevention of DGE following pancreatic surgery is thus suggested. A randomized, placebo-controlled report<sup>[88]</sup>, however, has questioned the role of octreotide in pancreaticoduodenectomy procedures. A similar study<sup>[89]</sup> showed that although octreotide use is associated with decreased rates of DGE compared with non-use, its use is significantly associated with the development of pancreatic fistulae. Based on their findings, the authors suggest avoidance of routine use of octreotide after pancreaticoduodenectomies until the development of international guidelines.

## IS DGE SIGNIFICANTLY ASSOCIATED WITH PPPD, BUT NOT WITH PD?

We searched the Medline/Pubmed database for clinical studies comparing the efficacy of PD *versus* PPPD with regards to DGE excluding publications not in the English language (Table 1). As a result, a total of 17 trials investigating the incidence of DGE after PPPD compared with PD are identified<sup>[6,12,20,25,34,63,66,73,77,90-97]</sup>. On the whole, 910 patients undergoing PD are compared with 1078 patients undergoing PPPD. Therefore, a total of 1988 patients have participated in these 17 studies.

Most early studies<sup>[12,25,63,90]</sup> showed that PD is superior to PPPD regarding incidence rates of DGE. However, only one study has demonstrated statistical significance in this outcome<sup>[25]</sup>. Another study showed that the difference in the occurrence rates of DGE after the two procedures is not significant because DGE when presents, resolves spontaneously within 6 wk. Later performed studies seem to support that the incidence rates of DGE following either PD or PPPD are comparable<sup>[34,63,66,73,77,91,93,95]</sup>, although supporters of PD over PPPD regarding DGE

rates also exist<sup>[94]</sup>. Some recent trials have even provided significantly lower rates of DGE following PPPD than following PD<sup>[92,96,97]</sup>.

The reasons behind this diversity are multifactorial. The definition of DGE following pancreatic surgery varies from study to study. Improvement of surgical technique and increased surgical experience as well as advances in perioperative and critical care management, have resulted in decreased rates of DGE in recent years. The degree of lymph node dissection and pancreatic resection as well as the performance of anastomoses vary in different centers. Peri-operative administration of drugs that have been shown to decrease post-operational rates of DGE, like octreotide or erythromycin lactobionate, varies from study to study. The indication for performing PD varies significantly not only between different studies, but also within the same patient cohort. There is therefore a growing need for a multicentre, randomized clinical trial with specific guidelines for peri-operative administration of pharmaceutical agents, standard definition of the term DGE, and specific etiology-based performance of pancreatic surgery, to compare the efficiency of the two methods regarding DGE.

## DISCUSSION

A recently reported modification in the classical PPPD procedure is the performance of duodenojejunostomy antecolically instead of retrocolically. Traverso and Kozuschek<sup>[98]</sup> reported a decade ago that antecolic duodenojejunostomy seems to be preferred by an increasing number of pancreatic surgery centers worldwide<sup>[61,69,99-101]</sup>. The theoretical background for this technique is that decreased blood circulation (especially venous drainage) of the jejunal limb following biliary-pancreato-enteric reconstructions can lead to decreased motility and profound edema of the jejunal limb itself, and eventually edema of the duodenojejunal anastomosis<sup>[27]</sup>. Compromised venous drainage of the jejunal limb, which is the peristalsis starting point of the newly constructed intestinal pathway, might lead to delayed recovery of jejunal peristalsis at the site of duodenojejunostomy, which will then cause DGE<sup>[62]</sup>. From a theoretical point of view, antecolic duodenojejunostomy avoids mechanical problems, because the descending jejunal loop is more mobile than after retrocolic reconstruction.

Kurosaki and Hatakeyama<sup>[99]</sup> evaluated the results of antecolic duodenojejunostomy in 55 consecutive patients undergoing PPPD as the selected mode of therapy for a wide variety of underlying diseases, and demonstrated that by use of the antecolic jejunal reconstruction method, DGE is markedly reduced based on the choice of the definition of DGE selected. According to the definition by Fabre *et al*<sup>[33]</sup>, DGE occurs in only 5.5% patients. According to the definition by van Berge Henegouwen *et al*<sup>[34]</sup>, DGE occurs in 29.1% patients, while according to the definition by Yeo *et al*<sup>[24]</sup>, DGE occurs in 18.2% patients.

These researchers demonstrated that the development of a major complication is correlated significantly with reinsertion of nasogastric tube or emesis ( $P = 0.010$ ), a later initiation of liquid diet ( $P = 0.0381$ ) and a later



Table 1 Association between DGE and PD/PPPD

Study	Yr	Patients (n)	Results
Klinkenbijn <i>et al</i> <sup>[20]</sup>	1992	91 (44 PDs, 47 PPPDs)	No difference with regards to DGE was demonstrated between the two groups (i.e. days to liquid and normal diet)
Roder <i>et al</i> <sup>[12]</sup>	1992	110 (62 PDs, 48 PPPDs)	DGE was noted in 0 (0%) patients after PD and 9 (19%) patients after PPPD ( <i>P</i> value not mentioned)
Patel <i>et al</i> <sup>[25]</sup>	1995	67 (52 PDs, 15 PPPDs)	DGE was noted in 41% of the PD group and 61% of the PPPD group ( <i>P</i> = 0.04)
Mosca <i>et al</i> <sup>[90]</sup>	1997	218 (61 PDs, 157 PPPDs)	DGE was noted in 1 (4.7%) patient after PD and 14 (8.9%) patients after PPPD ( <i>P</i> value not mentioned).
van Berge Henegouwen <i>et al</i> <sup>[34]</sup>	1997	200 (100 PDs, 100 PPPDs)	DGE was noted in 34 patients after PD and 37 patients after PPPD ( <i>P</i> = NS) <sup>1</sup>
Lin and Lin <sup>[63]</sup>	1999	30 (15 PDs, 15 PPPDs)	DGE was noted in 1 patient after PD and 6 patients after PPPD ( <i>P</i> = 0.08, two-sided Fisher's exact test, NS)
Di Carlo <i>et al</i> <sup>[91]</sup>	1999	113 (39 PDs, 74 PPPDs)	DGE was noted in 6 (15.3%) patients after PD and 9 (12.1%) patients after PPPD ( <i>P</i> = NS)
Yeo <i>et al</i> <sup>[92]</sup>	1999	106 (58 PDs, 48 PPPDs) <sup>2</sup>	DGE was noted in 9 (16%) patients after PD and 2 (4%) patients after PPPD ( <i>P</i> = 0.03)
Seiler <i>et al</i> <sup>[93]</sup>	2000	77 (40 PDs, 37 PPPDs)	DGE was noted in 18 (45%) patients after PD and 12 (32%) patients after PPPD ( <i>P</i> = 0.17, NS)
Martignoni <i>et al</i> <sup>[66]</sup>	2000	62 (27 PDs, 35 PPPDs)	DGE was noted in 9 (33%) patients after PD and 13 (37%) patients after PPPD ( <i>P</i> = NS)
Yamaguchi <i>et al</i> <sup>[94]</sup>	2001	50 (27 PDs, 23 PPPDs)	DGE was significantly associated with PPPD compared with PD (gastric tube removal, <i>P</i> < 0.0001, oral intake, <i>P</i> = 0.0018)
Yeo <i>et al</i> <sup>[6]</sup>	2002	294 (148 PDs, 146 PPPDs)	DGE was noted in 24 (16%) patients after PD and 9 (6%) patients after PPPD ( <i>P</i> = 0.006)
Nguyen <i>et al</i> <sup>[95]</sup>	2003	105 (50 PDs, 55 PPPDs) <sup>3</sup>	DGE was noted in 6 of 50 (12%) patients after PD and 4 of 55 (7%) patients after PPPD ( <i>P</i> = 0.40, NS)
Horstmann <i>et al</i> <sup>[73]</sup>	2004	132 (19 PDs, 113 PPPDs) <sup>4</sup>	DGE was noted in 4 of 19 (21%) patients after PD and 13 of 113 (12%) patients after PPPD ( <i>P</i> = 0.11, NS)
Tran <i>et al</i> <sup>[77]</sup>	2004	170 (83 PDs, 87 PPPDs) <sup>5</sup>	DGE was noted in 18 patients after PD and 19 patients after PPPD ( <i>P</i> = 0.80, NS)
Seiler <i>et al</i> <sup>[96]</sup>	2005	130 (66 PDs, 64 PPPDs)	DGE was noted in 30 (45%) patients after PD and 20 (31%) patients after PPPD ( <i>P</i> = 0.096, NS)
Lin <i>et al</i> <sup>[97]</sup>	2005	33 (19 PDs, 14 PPPDs) <sup>6</sup>	DGE was noted in 6 (43%) patients after PD and 0 patients after PPPD ( <i>P</i> < 0.05)

NS: Not significant. <sup>1</sup>Although nasogastric intubation was prolonged after PPPD *vs* PD (3 *vs* 6 d, *P* < 0.0001), this did not influence DGE rates; <sup>2</sup>Initially 114 patients were included in the study. Of these, 58 underwent PD while the remaining 56 were scheduled for PPPD. However, in 8 patients, the pylorus could not be preserved. They were therefore not included in the results; <sup>3</sup>In 7 of 55 (13%) patients in the PPPD group, the pylorus could not be preserved; <sup>4</sup>A total of 150 patients were included in the study but the 18 patients that underwent duodenum-preserving pancreatic head resection were not included here; <sup>5</sup>Two patients in the PPPD group were converted to the PD group during operation as the surgeon expected duodenal involvement; <sup>6</sup>Initially 36 patients were included in the study. Three patients with pancreatic head adenocarcinoma initially assigned to the PPPD group, had to undergo PD eventually due to extensive duodenal involvement. These 3 patients were not calculated in either study groups.

progression to solid diet (*P* = 0.0343). Furthermore, a major complication is correlated significantly with DGE but only according to the definition of DGE by Yeo *et al*<sup>[24]</sup> (*P* = 0.0006), and not according to the definition of DGE by Fabre *et al*<sup>[33]</sup> (*P* = 0.421) or van Berge Henegouwen *et al*<sup>[34]</sup> (*P* = 0.103). A major complication is defined as a condition requiring invasive treatment or intensive care, or a pancreatic fistula proved by amylase-rich (> 1000 mg/dL) fluid from drains over 7 postoperative days or radiological examination. In their group, 10 patients developed a major complication (five patients required intensive care or invasive treatment, while another 5 developed a pancreatic fistula).

In addition, division of the left gastric vein (LGV) is correlated significantly with the occurrence of DGE (5.3% *vs* 37%, if the LGV is preserved or divided, respectively, *P* = 0.0016) according to the definition of DGE by van Berge Henegouwen *et al*<sup>[34]</sup> but not according to the definition of DGE by Yeo *et al*<sup>[24]</sup> (0% *vs* 5%, if the LGV is preserved or divided, respectively, *P* = 0.067). After summing up their results, the authors concluded that, by

setting the stomach vertically in the left abdomen, antecolic duodenojejunostomy improves the occurrence of DGE after PPPD.

The decreased incidence of DGE following antemesenteric instead of retromesenteric jejunal reconstruction has been verified by other researchers as well. Park and associates<sup>[62]</sup> demonstrated that antemesenteric jejunal reconstruction is associated with a significantly lower incidence of DGE compared to retromesenteric reconstruction (6.5% *vs* 31.7%, respectively, *P* < 0.05) in terms of duration and amount of nasogastric drainage, as well as diet progression. Sugiyama and associates<sup>[100]</sup> also support the superiority of antemesenteric jejunal reconstruction with regards to DGE (8% *vs* 72% incidence of DGE for antemesenteric *vs* retromesenteric jejunal reconstruction respectively, *P* < 0.001). Horstmann and colleagues<sup>[73]</sup> demonstrated that performance of antecolic duodenojejunostomy-PPPD is associated with reduced (though not statistically significant) rates of DGE compared with standard Whipple (12% *vs* 21% for antecolic duodenojejunostomy-PPPD and

standard Whipple procedure respectively,  $P = 0.11$ ).

So far, a major drawback of all reported studies is the lack of randomization. Their interpretation has therefore noticeable limitations. Recently however, two randomized controlled trials have verified the positive effect of the antecolic reconstruction method on DGE rates<sup>[102,103]</sup>. The first study<sup>[102]</sup> reported a significantly lower incidence of DGE after antecolic compared with retrocolic duodenojejunostomy (5% vs 50% respectively,  $P = 0.0014$ ). However, due to the small number of patients included in this study ( $n = 20$  patients/group), the authors support that larger-scale studies are needed to confirm the positive results of this new reconstruction method. The second study<sup>[103]</sup> demonstrated the same positive results (5.0% vs 24.0% for antecolic and retrocolic duodenojejunostomy, respectively, Odds Ratio: 0.167, 95% CI: 0.054-0.430,  $P < 0.001$ ). Although the number of patients included in this trial was not as small ( $n = 100$  patients/group)<sup>[103]</sup> as in the first study<sup>[102]</sup>, a significant drawback is the difference in the time periods of sample collection (from January 1, 1996 until December 31, 2001 for the retromesenteric group, and from January 1, 2002 until December 31, 2003 for the antemesenteric group). Standardization of the operative technique, as well as continuous improvement in perioperative management, could account in part for the difference observed in DGE rates.

## CONCLUSION

Pylorus-preserving pancreatic head resection and classical Whipple are equal operations regarding the postoperative development of delayed gastric emptying. Further randomized controlled trials are required to confirm the advantage of antecolic versus retrocolic duodenojejunostomy in PPPD.

## REFERENCES

- Kausch W. Das carcinom der papilla duodeni und seine radikale Entfernung. *Beitr Z Clin Chir* 1912; **78**: 439-486
- Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. *Ann Surg* 1935; **102**: 763-779
- Whipple AO. The rationale for cancer of the pancreas and ampullary region. *Ann Surg* 1941; **114**: 612-615
- Trimble IR, Parsons WB, Sherman CP. A one-stage operation for the cure of carcinoma of the ampulla of Vater and the head of the pancreas. *Surg Gynecol Obstet* 1941; **73**: 711-722
- Grace PA, Pitt HA, Longmire WP. Pylorus preserving pancreatoduodenectomy: an overview. *Br J Surg* 1990; **77**: 968-974
- Yeo CJ, Cameron JL, Lillemoe KD, Sohn TA, Campbell KA, Sauter PK, Coleman J, Abrams RA, Hruban RH. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. *Ann Surg* 2002; **236**: 355-666; discussion 366-368
- Braasch JW, Gagner M. Pylorus-preserving pancreatoduodenectomy--technical aspects. *Langenbecks Arch Chir* 1991; **376**: 50-58
- Traverso LW, Longmire WP Jr. Preservation of the pylorus in pancreaticoduodenectomy. *Surg Gynecol Obstet* 1978; **146**: 959-962
- Traverso LW, Longmire WP Jr. Preservation of the pylorus in pancreaticoduodenectomy a follow-up evaluation. *Ann Surg* 1980; **192**: 306-310
- Watson K. Carcinoma of the ampulla of Vater: successful radical resection. *Br J Surg* 1944; **31**: 368-373
- McAfee MK, van Heerden JA, Adson MA. Is proximal pancreatoduodenectomy with pyloric preservation superior to total pancreatectomy? *Surgery* 1989; **105**: 347-351
- Roder JD, Stein HJ, Huttli W, Siewert JR. Pylorus-preserving versus standard pancreaticoduodenectomy: an analysis of 110 pancreatic and periampullary carcinomas. *Br J Surg* 1992; **79**: 152-155
- Newman KD, Braasch JW, Rossi RL, O'Campo-Gonzales S. Pyloric and gastric preservation with pancreatoduodenectomy. *Am J Surg* 1983; **145**: 152-156
- Braasch JW, Gongliang J, Rossi RL. Pancreatoduodenectomy with preservation of the pylorus. *World J Surg* 1984; **8**: 900-905
- Braasch JW, Deziel DJ, Rossi RL, Watkins E Jr, Winter PF. Pyloric and gastric preserving pancreatic resection. Experience with 87 patients. *Ann Surg* 1986; **204**: 411-418
- Hunt DR, McLean R. Pylorus-preserving pancreatectomy: functional results. *Br J Surg* 1989; **76**: 173-176
- Pearlman NW, Stiegmann GV, Ahnen DJ, Schultz AL, Fink LM. Acid and gastrin levels following pyloric-preserving pancreaticoduodenectomy. *Arch Surg* 1986; **121**: 661-664
- Patti MG, Pellegrini CA, Way LW. Gastric emptying and small bowel transit of solid food after pylorus-preserving pancreaticoduodenectomy. *Arch Surg* 1987; **122**: 528-532
- Kim HC, Suzuki T, Kajiwara T, Miyashita T, Imamura M, Tobe T. Exocrine and endocrine stomach after gastroduodenal preserving pancreatoduodenectomy. *Ann Surg* 1987; **206**: 717-727
- Klinkenbijn JH, van der Schelling GP, Hop WC, van Pel R, Bruining HA, Jeekel J. The advantages of pylorus-preserving pancreatoduodenectomy in malignant disease of the pancreas and periampullary region. *Ann Surg* 1992; **216**: 142-145
- Sharp KW, Ross CB, Halter SA, Morrison JG, Richards WO, Williams LF, Sawyers JL. Pancreatoduodenectomy with pyloric preservation for carcinoma of the pancreas: a cautionary note. *Surgery* 1989; **105**: 645-653
- Warshaw AL, Torchiana DL. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. *Surg Gynecol Obstet* 1985; **160**: 1-4
- Itani KM, Coleman RE, Meyers WC, Akwari OE. Pylorus-preserving pancreatoduodenectomy. A clinical and physiologic appraisal. *Ann Surg* 1986; **204**: 655-664
- Yeo CJ, Barry MK, Sauter PK, Sostre S, Lillemoe KD, Pitt HA, Cameron JL. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo-controlled trial. *Ann Surg* 1993; **218**: 229-237; discussion 237-238
- Patel AG, Toyama MT, Kusske AM, Alexander P, Ashley SW, Reber HA. Pylorus-preserving Whipple resection for pancreatic cancer. Is it any better? *Arch Surg* 1995; **130**: 838-842; discussion 842-843
- Miedema BW, Sarr MG, van Heerden JA, Nagorney DM, McIlrath DC, Ilstrup D. Complications following pancreaticoduodenectomy. Current management. *Arch Surg* 1992; **127**: 945-949; discussion 949-950
- Bar-Natan M, Larson GM, Stephens G, Massey T. Delayed gastric emptying after gastric surgery. *Am J Surg* 1996; **172**: 24-28
- Zerbi A, Balzano G, Patuzzo R, Calori G, Braga M, Di Carlo V. Comparison between pylorus-preserving and Whipple pancreatoduodenectomy. *Br J Surg* 1995; **82**: 975-979
- Yeo CJ. Pancreatic cancer: 1998 update. *J Am Coll Surg* 1998; **187**: 429-442
- Cameron JL. Whipple or pylorus preservation? A critical reappraisal and some new insights into pancreaticoduodenectomy. *Ann Surg* 2000; **231**: 301-302
- Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, Hruban RH, Ord SE, Sauter PK, Coleman J, Zahurak ML, Grochow LB, Abrams RA. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications,

- and outcomes. *Ann Surg* 1997; **226**: 248-257; discussion 257-260
- 32 **Balcom JH 4th**, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch Surg* 2001; **136**: 391-398
  - 33 **Fabre JM**, Burgel JS, Navarro F, Boccarat G, Lemoine C, Domergue J. Delayed gastric emptying after pancreaticoduodenectomy and pancreaticogastrostomy. *Eur J Surg* 1999; **165**: 560-565
  - 34 **van Berge Henegouwen MI**, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H, Gouma DJ. Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: an analysis of 200 consecutive patients. *J Am Coll Surg* 1997; **185**: 373-379
  - 35 **Harkness GA**, Bentley DW, Roghmann KJ. Risk factors for nosocomial pneumonia in the elderly. *Am J Med* 1990; **89**: 457-463
  - 36 **Dooley CP**, Reznick JB, Valenzuela JE. Variations in gastric and duodenal motility during gastric emptying of liquid meals in humans. *Gastroenterology* 1984; **87**: 1114-1119
  - 37 **Azpiroz F**. Control of gastric emptying by gastric tone. *Dig Dis Sci* 1994; **39**: 185-195
  - 38 **Haba T**, Sarna SK. Regulation of gastroduodenal emptying of solids by gastropyloroduodenal contractions. *Am J Physiol* 1993; **264**: G261-G271
  - 39 **Holzer HH**, Raybould HE. Vagal and splanchnic sensory pathways mediate inhibition of gastric motility induced by duodenal distension. *Am J Physiol* 1992; **262**: G603-G608
  - 40 **Cooke AR**. Control of gastric emptying and motility. *Gastroenterology* 1975; **68**: 804-816
  - 41 **Beglinger C**. Effect of cholecystokinin on gastric motility in humans. *Ann N Y Acad Sci* 1994; **713**: 219-225
  - 42 **Yamagishi T**, Debas HT. Cholecystokinin inhibits gastric emptying by acting on both proximal stomach and pylorus. *Am J Physiol* 1978; **234**: E375-E378
  - 43 **Liddle RA**, Morita ET, Conrad CK, Williams JA. Regulation of gastric emptying in humans by cholecystokinin. *J Clin Invest* 1986; **77**: 992-996
  - 44 **Holzer HH**, Turkelson CM, Solomon TE, Raybould HE. Intestinal lipid inhibits gastric emptying via CCK and a vagal capsaicin-sensitive afferent pathway in rats. *Am J Physiol* 1994; **267**: G625-629
  - 45 **Fraser R**, Fone D, Horowitz M, Dent J. Cholecystokinin octapeptide stimulates phasic and tonic pyloric motility in healthy humans. *Gut* 1993; **34**: 33-37
  - 46 **Muller MW**, Friess H, Beger HG, Kleeff J, Lauterburg B, Glasbrenner B, Riepl RL, Buchler MW. Gastric emptying following pylorus-preserving Whipple and duodenum-preserving pancreatic head resection in patients with chronic pancreatitis. *Am J Surg* 1997; **173**: 257-263
  - 47 **Hopman WP**, Jansen JB, Lamers CB. Plasma cholecystokinin response to oral fat in patients with Billroth I and Billroth II gastrectomy. *Ann Surg* 1984; **199**: 276-280
  - 48 **Meyer BM**, Werth BA, Beglinger C, Hildebrand P, Jansen JB, Zach D, Rovati LC, Stalder GA. Role of cholecystokinin in regulation of gastrointestinal motor functions. *Lancet* 1989; **2**: 12-15
  - 49 **Tangoku A**, Nishikawa M, Adachi A, Suzuki T. Plasma gastrin and cholecystokinin response after pylorus-preserving pancreatoduodenectomy with Billroth-I type of reconstruction. *Ann Surg* 1991; **214**: 56-60
  - 50 **Kleibeuker JH**, Beekhuis H, Piers DA, Schaffalitzky de Muckadell OB. Retardation of gastric emptying of solid food by secretin. *Gastroenterology* 1988; **94**: 122-126
  - 51 **McTigue DM**, Rogers RC. Pancreatic polypeptide stimulates gastric motility through a vagal-dependent mechanism in rats. *Neurosci Lett* 1995; **188**: 93-96
  - 52 **Adler G**, Beglinger C, Braun U, Reinshagen M, Koop I, Schafmayer A. Cholecystokinin is a regulator of intestinal phase-stimulated PP release. *Regul Pept* 1990; **30**: 105-111
  - 53 **Riepl RL**, Fiedler F, Ernstberger M, Teufel J, Lehnert P. Effect of intraduodenal taurodeoxycholate and L-phenylalanine on pancreatic secretion and on gastroenteropancreatic peptide release in man. *Eur J Med Res* 1996; **1**: 499-505
  - 54 **Malfertheiner P**, Sarr MG, Spencer MP, DiMagno EP. Effect of duodenectomy on interdigestive pancreatic secretion, gastrointestinal motility, and hormones in dogs. *Am J Physiol* 1989; **257**: G415-G422
  - 55 **Lamers CB**, Diemel CM, Jansen JB. Serum pancreatic polypeptide responses to food and secretion in patients with Billroth I and Billroth II gastrectomies and in normal subjects. *Surgery* 1982; **91**: 288-292
  - 56 **Miller LJ**, Clain JE, Malagelada JR, Go VL. Control of human postprandial pancreatic exocrine secretion: a function of the gastroduodenal region. *Dig Dis Sci* 1979; **24**: 150-154
  - 57 **Meeroff JC**, Go VL, Phillips SF. Control of gastric emptying by osmolality of duodenal contents in man. *Gastroenterology* 1975; **68**: 1144-1151
  - 58 **Tanaka M**, Sarr MG. Role of the duodenum in the control of canine gastrointestinal motility. *Gastroenterology* 1988; **94**: 622-629
  - 59 **Malfertheiner P**, Sarr MG, Nelson DK, DiMagno EP. Role of the duodenum in postprandial release of pancreatic and gastrointestinal hormones. *Pancreas* 1994; **9**: 13-19
  - 60 **Tanaka M**, Sarr MG. Total duodenectomy: effect on canine gastrointestinal motility. *J Surg Res* 1987; **42**: 483-493
  - 61 **Hocking MP**, Harrison WD, Sninsky CA. Gastric dysrhythmias following pylorus-preserving pancreaticoduodenectomy. Possible mechanism for early delayed gastric emptying. *Dig Dis Sci* 1990; **35**: 1226-1230
  - 62 **Park YC**, Kim SW, Jang JY, Ahn YJ, Park YH. Factors influencing delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. *J Am Coll Surg* 2003; **196**: 859-865
  - 63 **Lin PW**, Lin YJ. Prospective randomized comparison between pylorus-preserving and standard pancreaticoduodenectomy. *Br J Surg* 1999; **86**: 603-607
  - 64 **Murakami H**, Suzuki H, Nakamura T. Pancreatic fibrosis correlates with delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy with pancreaticogastrostomy. *Ann Surg* 2002; **235**: 240-245
  - 65 **Kim DK**, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H, Grendell JH, Reed WP. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreatoduodenectomy? *Ann Surg Oncol* 2005; **12**: 222-227
  - 66 **Martignoni ME**, Friess H, Sell F, Ricken L, Shrikhande S, Kulli C, Buchler MW. Enteral nutrition prolongs delayed gastric emptying in patients after Whipple resection. *Am J Surg* 2000; **180**: 18-23
  - 67 **Ueno T**, Tanaka A, Hamaoka Y, Tsurumi M, Suzuki T. A proposal mechanism of early delayed gastric emptying after pylorus preserving pancreatoduodenectomy. *Hepatogastroenterology* 1995; **42**: 269-274
  - 68 **Tanaka A**, Ueno T, Oka M, Suzuki T. Effect of denervation of the pylorus and transection of the duodenum on acetaminophen absorption in rats; possible mechanism for early delayed gastric emptying after pylorus preserving pancreatoduodenectomy. *Tohoku J Exp Med* 2000; **192**: 239-247
  - 69 **Goei TH**, Henegouwen MI, Slooff MJ, van Gulik TM, Gouma DJ, Eddes EH. Pylorus-preserving pancreatoduodenectomy: influence of a Billroth I versus a Billroth II type of reconstruction on gastric emptying. *Dig Surg* 2001; **18**: 376-380
  - 70 **Bassi C**, Falconi M, Molinari E, Salvia R, Butturini G, Sartori N, Mantovani W, Pederzoli P. Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. *Ann Surg* 2005; **242**: 767-771, discussion 771-773
  - 71 **Takao S**, Shimazu H, Maenohara S, Shintchi H, Aikou T. Modified pancreaticogastrostomy following pancreaticoduodenectomy. *Am J Surg* 1993; **165**: 317-321
  - 72 **Bassi C**, Falconi M, Molinari E, Mantovani W, Butturini G, Gumbs AA, Salvia R, Pederzoli P. Duct-to-mucosa versus end-to-side pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: results of a prospective randomized trial. *Surgery* 2003; **134**: 766-771
  - 73 **Horstmann O**, Markus PM, Ghadimi MB, Becker H. Pylorus

- preservation has no impact on delayed gastric emptying after pancreatic head resection. *Pancreas* 2004; **28**: 69-74
- 74 **Riediger H**, Makowiec F, Schareck WD, Hopt UT, Adam U. Delayed gastric emptying after pylorus-preserving pancreatoduodenectomy is strongly related to other postoperative complications. *J Gastrointest Surg* 2003; **7**: 758-765
  - 75 **Kimura F**, Suwa T, Sugiura T, Shinoda T, Miyazaki M, Itoh H. Sepsis delays gastric emptying following pylorus-preserving pancreaticoduodenectomy. *Hepatogastroenterology* 2002; **49**: 585-588
  - 76 **Horstmann O**, Becker H, Post S, Nustede R. Is delayed gastric emptying following pancreaticoduodenectomy related to pylorus preservation? *Langenbecks Arch Surg* 1999; **384**: 354-359
  - 77 **Tran KT**, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW, Terpstra OT, Zijlstra JA, Klinkert P, Jeekel H. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. *Ann Surg* 2004; **240**: 738-745
  - 78 **Suzuki H**, Mochiki E, Haga N, Shimura T, Itoh Z, Kuwano H. Effect of duodenectomy on gastric motility and gastric hormones in dogs. *Ann Surg* 2001; **233**: 353-359
  - 79 **Peeters TL**, Bormans V, Vantrappen G. Comparison of motilin binding to crude homogenates of human and canine gastrointestinal smooth muscle tissue. *Regul Pept* 1988; **23**: 171-182
  - 80 **Kondo Y**, Torii K, Itoh Z, Omura S. Erythromycin and its derivatives with motilin-like biological activities inhibit the specific binding of 125I-motilin to duodenal muscle. *Biochem Biophys Res Commun* 1988; **150**: 877-882
  - 81 **Itoh Z**, Nakaya M, Suzuki T, Arai H, Wakabayashi K. Erythromycin mimics exogenous motilin in gastrointestinal contractile activity in the dog. *Am J Physiol* 1984; **247**: G688-G694
  - 82 **Tack J**, Janssens J, Vantrappen G, Peeters T, Annese V, Depoortere I, Muls E, Bouillon R. Effect of erythromycin on gastric motility in controls and in diabetic gastroparesis. *Gastroenterology* 1992; **103**: 72-79
  - 83 **Janssens J**, Peeters TL, Vantrappen G, Tack J, Urbain JL, De Roo M, Muls E, Bouillon R. Improvement of gastric emptying in diabetic gastroparesis by erythromycin. Preliminary studies. *N Engl J Med* 1990; **322**: 1028-1031
  - 84 **Ohwada S**, Satoh Y, Kawate S, Yamada T, Kawamura O, Koyama T, Yoshimura S, Tomizawa N, Ogawa T, Morishita Y. Low-dose erythromycin reduces delayed gastric emptying and improves gastric motility after Billroth I pylorus-preserving pancreaticoduodenectomy. *Ann Surg* 2001; **234**: 668-674
  - 85 **Harris AG**. Somatostatin and somatostatin analogues: pharmacokinetics and pharmacodynamic effects. *Gut* 1994; **35**: S1-S4
  - 86 **Buchler M**, Friess H, Klempa I, Hermanek P, Sulkowski U, Becker H, Schafmayer A, Baca I, Lorenz D, Meister R. Role of octreotide in the prevention of postoperative complications following pancreatic resection. *Am J Surg* 1992; **163**: 125-130; discussion 130-131
  - 87 **van Berge Henegouwen MI**, van Gulik TM, Akkermans LM, Jansen JB, Gouma DJ. The effect of octreotide on gastric emptying at a dosage used to prevent complications after pancreatic surgery: a randomised, placebo controlled study in volunteers. *Gut* 1997; **41**: 758-762
  - 88 **Yeo CJ**, Cameron JL, Lillemoe KD, Sauter PK, Coleman J, Sohn TA, Campbell KA, Choti MA. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. *Ann Surg* 2000; **232**: 419-429
  - 89 **Moon HJ**, Heo JS, Choi SH, Joh JW, Choi DW, Kim YI. The efficacy of the prophylactic use of octreotide after a pancreaticoduodenectomy. *Yonsei Med J* 2005; **46**: 788-793
  - 90 **Mosca F**, Giulianotti PC, Balestracci T, Di Candio G, Pietrabissa A, Sbrana F, Rossi G. Long-term survival in pancreatic cancer: pylorus-preserving versus Whipple pancreaticoduodenectomy. *Surgery* 1997; **122**: 553-566
  - 91 **Di Carlo V**, Zerbi A, Balzano G, Corso V. Pylorus-preserving pancreaticoduodenectomy versus conventional whipple operation. *World J Surg* 1999; **23**: 920-925
  - 92 **Yeo CJ**, Cameron JL, Sohn TA, Coleman J, Sauter PK, Hruban RH, Pitt HA, Lillemoe KD. Pancreaticoduodenectomy with or without extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma: comparison of morbidity and mortality and short-term outcome. *Ann Surg* 1999; **229**: 613-622; discussion 622-624
  - 93 **Seiler CA**, Wagner M, Sadowski C, Kulli C, Buchler MW. Randomized prospective trial of pylorus-preserving vs. Classic duodenopancreatectomy (Whipple procedure): initial clinical results. *J Gastrointest Surg* 2000; **4**: 443-452
  - 94 **Yamaguchi K**, Kishinaka M, Nagai E, Nakano K, Ohtsuka T, Chijiwa K, Tanaka M. Pancreatoduodenectomy for pancreatic head carcinoma with or without pylorus preservation. *Hepatogastroenterology* 2001; **48**: 1479-1485
  - 95 **Nguyen TC**, Sohn TA, Cameron JL, Lillemoe KD, Campbell KA, Coleman J, Sauter PK, Abrams RA, Hruban RH, Yeo CJ. Standard vs. radical pancreaticoduodenectomy for periampullary adenocarcinoma: a prospective, randomized trial evaluating quality of life in pancreaticoduodenectomy survivors. *J Gastrointest Surg* 2003; **7**: 1-9; discussion 9-11
  - 96 **Seiler CA**, Wagner M, Bachmann T, Redaelli CA, Schmied B, Uhl W, Friess H, Buchler MW. Randomized clinical trial of pylorus-preserving duodenopancreatectomy versus classical Whipple resection-long term results. *Br J Surg* 2005; **92**: 547-556
  - 97 **Lin PW**, Shan YS, Lin YJ, Hung CJ. Pancreaticoduodenectomy for pancreatic head cancer: PPPD versus Whipple procedure. *Hepatogastroenterology* 2005; **52**: 1601-1604
  - 98 **Traverso LW**, Kozuschek RA. Long term follow-up after pylorus-preserving pancreatico-duodenectomy for severe complications of chronic pancreatitis. *Dig Surg* 1996; **13**: 118-126
  - 99 **Kurosaki I**, Hatakeyama K. Preservation of the left gastric vein in delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. *J Gastrointest Surg* 2005; **9**: 846-852
  - 100 **Sugiyama M**, Abe N, Ueki H, Masaki T, Mori T, Atomi Y. A new reconstruction method for preventing delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. *Am J Surg* 2004; **187**: 743-746
  - 101 **Kurosaki I**, Hatakeyama K. Clinical and surgical factors influencing delayed gastric emptying after pyloric-preserving pancreaticoduodenectomy. *Hepatogastroenterology* 2005; **52**: 143-148
  - 102 **Tani M**, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K, Yamaue H. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. *Ann Surg* 2006; **243**: 316-320
  - 103 **Hartel M**, Wente MN, Hinz U, Kleeff J, Wagner M, Muller MW, Friess H, Buchler MW. Effect of antecolic reconstruction on delayed gastric emptying after the pylorus-preserving Whipple procedure. *Arch Surg* 2005; **140**: 1094-1099

S- Editor Wang J L- Editor Wang XL E- Editor Bi L