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TITLE: Pancreaticogastrostomy .... Seven years Tertiary Hospital Experience

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Short Running Title: NOT GIVEN

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**ABSTRACT**

**Aims**
Pancreaticoduodenectomy (PD) is the treatment of choice for periampullary tumors. However, this procedure carries significant risk and potential morbidity, mostly related to pancreatic anastomotic failure. Many techniques have been described in an attempt to decrease the anastomotic leak rate and related complications. Pancreaticogastrostomy (PG) is one of the techniques utilized to restore pancreatic continuity after pancreatic head resection.

The aim of this study is to share our experience with the pancreaticogastrostomy technique.

**Design**
Retrospective review of all patients who underwent pancreaticoduodenectomy between 2008 to August 2015 at King Faisal Specialist Hospital & Research Center (Gen. Org.)-Jeddah, Kingdom of Saudi Arabia.

**Methods**
A total of 36 patients underwent a pancreaticoduodenectomy with a pancreaticogastrostomy using our modified technique. Variables studied included indications for surgery, intra-operative and post-operative factors and post-operative complications.

**Results**
At King Faisal Specialist Hospital & Research Center (Gen. Org.)-Jeddah in group of patients who underwent pancreaticogastrostomy (n=36) including 21 males and 15 females, the mean age was 58.44 years (SD 15.76). The histopathology review post operatively showed 7 benign cases and 29 malignant cases. The indications for pancreaticoduodenectomy based on the histopathology have been divided into 7 main categories: adenocarcinomas, neuroendocrine tumors, intra-ductal tumors,
pseudopapillary tumors, cystic lesions of the pancreas, trauma and others including inflammations and fibrosis. The mean tumor size was 3.29 cm in diameter (range, 0-11 cm) with (0-6) no of lymph node involvement. There was a vascular invasion in 23.5% of the cases. The highest morbidity in our series following pancreaticoduodenectomy was, wound infection (22.2%), atelectasis (13.9%), delayed gastric emptying and postoperative bleeding (8.3%). Others include Intra-operative and post-operative hemorrhage, abscesses and collections, wound dehiscence and Pulmonary embolism (PE) counted for 5.6% of the complications. Intraoperative bleeding, pancreatic fistula, biliary fistulas, Lymphatic duct injury and deep venous thrombosis (DVT) occurred in 2.8% of the patients.

**Conclusion**

Pancreatic stump invagination into the gastric lumen with a two layers fixation of the ventral surface of the pancreas might be associated with a lower risk of pancreatic anastomosis failure compared with other techniques. Further prospective validation with a larger number of cases are needed to support our results.

**Keywords:** NOT GIVEN
INTRODUCTION

The 5 year survival rate of pancreatic cancer is the lowest among all cancer types. Early diagnosis is essential and the only chance for cure is resection [1,2]. Up to 85% of patients with pancreatic cancer are already in advanced stage at the time of the diagnosis and in those patients curative resection is possible in only 10-15% [1].

PD is the procedure of choice for all periampullary tumors and pancreatic head tumors, specifically [1]. Although the mortality rate following PD is reported to be around 3-5% only [1], post-operative morbidity is still relatively high (20-30%) despite improvements over recent years [4]. PD is an invasive and potentially risky procedure and a key step is anastomoses of the pancreatic remnant to the intestine [5]. Various techniques for managing the pancreatic remnant have been reported including simple ligation of the pancreatic duct [6,7], occlusion of the pancreatic duct using a synthetic rubber injection or fibrin glue [8,9], optimization of the blood supply of the edge of the pancreatic remnant and meticulous placement of sutures using magnification [10], application of fibrin glue sealant around the pancreaticojejunal (PJ) anastomosis [11], various modifications of the PJ (either end-to-end or end-to-side anastomosis) [12,13] or isolated Roux-en-Y pancreaticojejunostomy [14,15]. Results following PG have been inconsistently reported in numerous studies [16,17]. Bassi et al showed that biliary fistula, postoperative collections and delayed gastric emptying were significantly reduced in patients treated by PG compared with alternative anastomoses [23]. In addition, PG is associated with lower frequency of multiple surgical complications. The purpose of the present study is to describe and evaluate our modified PG technique on 36 patients in a retrospective manner to determine whether this is a safe procedure for managing restoration of pancreatic remnant.

MATERIALS AND METHODS

We conducted a retrospective review of 36 patients who underwent PG after PD at King Faisal Specialist Hospital & Research Center (Gen. Org.)-Jeddah, KSA
between 2008 and August 2015. All procedures were conducted by a single surgeon (Dr. Saud Al-Muhammadi (S.A.)).

All patients were investigated pre-operatively to confirm their diagnosis and to evaluate their general and nutritional health statistics. Blood work, electrocardiogram (ECG), Chest X-ray and an abdomen and pelvis computed tomography (CT) scan were performed for all patients.

Clinical and pathological data were obtained from the hospital data base and medical records. Data obtained for each patient included demographics, preoperative laboratory values, pre-operative intervention, intraoperative data such as the use of prophylactic antibiotics, the use of intravenous octreotide before the anastomosis, the length of the operation and the blood loss.

Post-operative data, included complications, pathological findings, and survival outcomes. Analyses were performed using statistical software (IBM SPSS statistics 21 for windows) with the t-test used where appropriate. Statistical significance was set at $P=.05$.

SURGICAL TECHNIQUE

The abdominal cavity was accessed via a longitudinal upper midline incision and, after stepwise mobilization, the PD performed. The pancreatic parenchymal transection was performed using cutting electrocutary after controlling the blood supply originating from 2 arterial arcades in front of and behind the pancreatic head using a 4-0 PDS suture.

Reconstruction of the PG was done using the most common technique described by Mackie and Rhoads involving a simple invagination technique with few modification. A two to two and half centimeter length of the remnant pancreas was mobilized from the surrounding tissues using ligature ties (almost always one to two splenic vein and arterial branches need to be ligated). Excessive mobilization of the pancreas was avoided to reduce the risk of pancreatic necrosis/pancreatitis.

A small incision was then made in the posterior surface of the stomach (the diameter of the gastric incision is calibrated to 1 cm less than the diameter of the pancreatic stump) and two invaginating sutures fixed to each corner of the gastrostomy incision.
These two sutures are responsible for invaginating the pancreas into the stomach and are an important step during this procedure (Figure 1). A row of interrupted 4-0 monofilament sutures is then placed between the gastric seromuscular layer and the anterior wall of the pancreatic parenchyma two centimetres from the cut edge of the pancreas. The suture is passed proximal to distal to improve invagination of 1-2cm of pancreatic parenchyma when tying these sutures (Figure 2). Sutures are then placed from the posteroinferior gastric wall to the posterior body of the pancreas, using the same technique of proximal to distal passage of the suture through the pancreas (Figure 3). A second continuous layer of sutures is then added to the posterior body of the pancreas and the inferior cut edge of the gastrostomy (Figure 4).

The hepaticojejunostomy and gastrojejunostomy are performed using a Roux-en Y technique with an interrupted single layer of PDS for the H-J and a stapled anastomosis for both the gastrojejunostomy and the enteroenterostomy. Two drains are left in place, one in the sub hepatic area and one below the pancreatic anastomosis. The abdominal cavity was closed using a running suture of loop #1 PDS. The skin was closed using a stapler. The median operation time was 6 hours, ranging between 2-11 hours. The median estimated blood loss 400 ml, ranging between 100-1500 ml.

POST OPERATIVE CARE

All patients were transferred to the surgical intensive care unit (SICU) for 24 hours post operatively. Prophylactic Intravenous (IV) Cefazolin (Kefazol®) 1gm every 8 hours and Metronidazole (Flazol®) 500 mg every 6 hours was given for seven days, Metoclopramide (Primperan®) 10 mg every 8 hours PRN for nausea and vomiting, Omeprazole (Losec®) 20 mg every 12 hours, all our patients received either patient controlled analgesia (PCA Fentanyl) (Sublimaz®) or epidural anesthesia for 3 days maximum. Acetaminophen (Perfalgan®) 500-1000 mg every 6 hours and Tramadol (Tramal®) 50-100 mg every 6 hours were used when the PCA or epidural anesthesia was removed, Octreotide (Sandostatin®) 100 mcg every 8 hours was given for 5 days. Patients received unfractionated heparin 5000 IU TID via a subcutaneous (SC) route as DVT prophylaxis.
Oral fluids were reintroduced on day 6 and then progressed to full diet, as tolerated. Delayed gastric emptying was diagnosed if the NGT aspirate remained high for 10 days or more, with or without persistent vomiting after removal of the NGT, or there was a need for reinsertion of the NGT or failure to progress to a regular diet. Both intra-abdominal drains were attached to vacuum containers and were monitored daily for volume output. Amylase levels from the serum and drainage fluid were measured on day 5. Any fluid level exceeding 10 ml or 3 times higher than the serum level was defined as a pancreatic leak. Bile leak was suspected whenever the drainage fluid became dark yellow or green in color. Fluid analysis was then done to confirm the presence of bilirubin.

RESULTS

In total, 36 patients underwent PG including 21 males and 15 females. The mean age of this cohort was 58.44 years (SD 15.76). Thirty six percent of patients had biliary stents placed pre-operatively via endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous drainage (PTC) of the biliary system under radiological guidance. Histopathological analysis confirmed 7 benign cases and 29 malignant cases as shown in Table 1. In this cohort the mean tumor size was 3.29 cm (range, 0-11 cm), of the malignant cases vascular invasion was seen in 23.5% of specimens. The mean operating time was 5.6 hours (SD 1.74), the mean intra operative blood loss was 676.39 ml (SD 1222.96). The mean hospital stay was 11.86 days (SD 6.05). The mean survival rate was 9.5 months (SD 11.68).

During the follow up period, four patients (11.1%) died 9 months to 4 years after the procedure. One patient was lost to follow up. In hospital mortality (define – is this 90 days) occurred in two patients (5.5%). One patient died from intra-operative bleeding as a result of a porta hepatis injury and the other died on day-1 due to DIC as a result of massive blood transfusion for intra-operative bleeding. The 2 patients were excluded from the final survival analysis.

The overall morbidity was 83.3% which included wound infections (22.2%), atelectasis (13.9%) and delayed gastric emptying and post-operative hemorrhage (8.3%). Abscesses and collections, wound dehiscence and PE occurred in a total of
(5.6%) of the cases. Intra-operative hemorrhage, Pancreatic and biliary fistulas, lymphatic duct injury and DVT account for (2.8%) of the complications. The lowest rate was (0%) in major complications such as cholangitis and acute pancreatitis (Table 2).

**DISCUSSION**

Periampullary tumors are defined as those arising from the head of the pancreas, the distal common bile duct and the duodenum. Overall they have a high mortality rate compared with other cancer types, and account for >30,000 cancer related deaths per year in the U.S. [19]. The most definite treatment for periampullary tumors is PD although this is still considered as a relatively risky procedure with a high morbidity and mortality rate. Post-operative morbidity occurs in up to 45.1% of cases [20]. The most significant complication is a pancreaticoenteric anastomotic leak which is reported to occur in 5%-20% of cases [15]. The presence of a pancreatic leak increases the mortality rate, Lerut et al reported that pancreatic fistula accounted for 55% of postoperative deaths [21]. PJ is the most commonly used technique for managing the pancreatic remnant. However when using this technique anastomotic leaks and pancreatic fistulas have been reported in up to 11-40% of cases [22,23]. Pancreaticoenteric anastomotic failure often results in delayed gastric emptying, pancreatic fistula, and wound infection. The consequences of a pancreatic fistula may be dire sometimes, leading to intra-abdominal hemorrhage, intra-abdominal infection, wound dehiscence and even death [24]. Yeo et al reported on outcomes after 650 consecutive PDs [25]. They noted that four percent of patients required repeat surgery and that one third of these patients died after the second operation as a result mostly related to leakage from the PJ anastomosis. The modified technique of PG used in the present series resulted in zero leaks and numerous other groups have similar good results using this technique, Miyagawa et al. [26] in a retrospective comparative study found that PG was superior to PJ in terms of anastomotic breakdown. Bartoli, [27] undertook a meta-analysis of pancreatic fistula and relative mortality in malignant disease after PD. They compared data on PG versus PJ anastomosis performed in three different ways, i.e., PJ end to side, PJ end to end, and Wirsung duct to jejunal end to side anastomosis. In all cases PG was associated
with lower morbidity and mortality rates compared with a PJ anastomosis. In a retrospective study on 214 patients Aranha GV et al showed a significant difference in mortality between the two groups in favour of the PG group [18]. Anastomoses of the pancreas was first described theoretically by Tripodi and Sherwin in 1934 [28]. The technique was further evaluated in the laboratory by Person and Glenn [29]. The first successful PG in a patient was performed by Waugh and Clagett in 1946 [30]. In a review done from 1946 to 1997 by Mason, pancreaticogastrostomy seems to be a safe procedure. A total of 199 cases using the PG technique were described in the literature. A mortality of 4.5% (9/199) and a leakage rate of 1% (2/199) were reported. None of the nine deaths described in this review were attributed to PG. During the time period 1991 to 1997, the number of PGs described in the literature was 614. The incidence of leakage for this period when compared with the previous period rose to 4.7% (29/614), with an overall mortality of 3.3% (20/614). In this mortality group only 15% of deaths were related to the PG anastomosis [31]. Numerous theories have been proposed as to why a PG might be more favorable in terms of the risk of an anastomotic leak compared with PJ. Firstly, the stomach is known to have a rich blood supply which might decrease the risk of ischemic complications. Secondly, the thick wall of the stomach makes the sutures hold better than in the jejunum. Thirdly, the pancreas lies immediately behind the stomach and anastomosing it in the posterior wall allows a tension free anastomosis which may reduce the risk of leakage. Fourthly, there is no accumulation of pancreaticobiliary secretions as presumably occurs in a long loop of the jejunum which can add tension to the anastomosis. Fifthly, the relatively acidic media of the stomach do not activate the pancreatic proteolytic enzymes which may also help protect the anastomosis. Lastly, the alkaline pancreatic secretions neutralize the gastric acidity which protects against potential marginal ulceration [20,32]. In addition to these, there are other controllable factors which can affect the anastomosis and the general outcome. These can be divided into: pancreatic factors, patient factors and operative factors. Pancreatic factors include [1] the pancreatic texture where the fibrotic pancreatic remnant is less likely to leak after an anastomosis compared with a soft and fragile pancreatic remnant; [2] the original pathology; [3] the blood supply to the pancreatic remnant; [4] and the pancreatic duct size. Patient related factors include: age,
gender, level of preoperative jaundice, and comorbid diseases. Operative factors include operation time, blood loss, type of anastomosis and stenting of the pancreatic duct [33]. Numerous pharmacological agents have been described to decrease or prevent pancreatic anastomotic leaks. The most commonly used medication is octreotide. A recent meta-analysis by Connor et al, showed that octreotide usage reduces the incidence of post-operative complications in pancreatic surgery [34].

CONCLUSION

pancreatic stump invagination into the gastric lumen for about 2cm with a two layer fixation of the ventral surface of the pancreas was associated with low risk of pancreatic anastomosis failure in our study. The limitations of this include the small sample size and the range of different pathologies in this series. Larger multi-centric studies are needed to establish whether PG reconstruction following PD is superior to PJ reconstruction.

CONFLICT OF INTEREST

NOT GIVEN

AUTHOR’S CONTRIBUTIONS

NOT GIVEN

REFERENCES


34. Connor S, Alexakis N, Garden DJ, Leandros E, Bramis J, Wigmore SJ. Meta-

FIGURE LEGENDS

Figure 1: Gastro-pancreatic corner mattress stitch, notice the stitch out-in 2cm above both gastrostomy corners and anterior-posterior through both superior and inferior edge of the pancreas 2cm below the cut edge of the pancreas.

Figure 2: Simple suture between superior edge of gastrostomy and dorsal service of pancreas, notice the stitch are taken through pancreatic service distal 2 cm below the cut edge of the pancreas.

Figure 3: Mattress suture out-in through the inferior edge of the gastrostomy and the ventral surface of the pancreas. Note, sutures are passed proximal to distal through the pancreas, 2cm away from the cut edge.

Figure 4: A continuous suture is placed between the inferior edge of the gastrotomy and the pancreatic tissue at the ventral surface to reinforce the posterior layer (after invaginating the pancreas into the stomach.
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Figure 4: A continuous suture is placed between the inferior edge of the gastrotomy and the pancreatic tissue at the ventral surface to reinforce the posterior layer (after invaginating the pancreas into the stomach.)
Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>58.44±15.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (58.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (41.6%)</td>
</tr>
<tr>
<td>Histopathological result</td>
<td></td>
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<tr>
<td>Adenocarcinoma</td>
<td>25 (69.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (8.3%)</td>
</tr>
<tr>
<td>Neuroendocrine tumour</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Cystic lesion</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Intraductal lesion</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>1 (2.7%)</td>
</tr>
<tr>
<td>Pseudo-papillary tumor</td>
<td>1 (2.7%)</td>
</tr>
<tr>
<td>Tumour size (cm)</td>
<td>3.29±(SD2.28)</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>8 (23.5%)</td>
</tr>
<tr>
<td>Absent</td>
<td>28 (77.7%)</td>
</tr>
<tr>
<td>Operating time (hours)</td>
<td>5.6±1.74</td>
</tr>
<tr>
<td>Intra operative blood loss (ml)</td>
<td>676.39±1222.96</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>11.86±6.05</td>
</tr>
<tr>
<td>Survival (months)</td>
<td>9.5±11.68</td>
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Table 2: Post-operative complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Wound infection</td>
<td>8</td>
<td>22.2%</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>5</td>
<td>13.9%</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>3</td>
<td>8.3%</td>
</tr>
<tr>
<td>Post-operative hemorrhage</td>
<td>3</td>
<td>8.3%</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>2</td>
<td>5.6%</td>
</tr>
<tr>
<td>Abscess or collection</td>
<td>2</td>
<td>5.9%</td>
</tr>
<tr>
<td>PE</td>
<td>2</td>
<td>5.6%</td>
</tr>
<tr>
<td>Intra-operative hemorrhage</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Biliary fistula</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Lymphatic duct injury</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>DVT</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
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<td>0%</td>
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