

## Clinical Analysis of Pancreatoduodenectomy with Duct-to-Mucosa Pancreaticojejunostomy; A Single-Center Report

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### Abstract

**Objective/Aims:** The study sought to analyze Whipple procedure in 65 patients' in-hospital evaluation of morbidity and mortality rate after pancreatoduodenectomy (PD) with adjusted duct-to mucosa pancreaticojejunostomy.

**Methods:** A retrospective study of 65 consecutive patients that underwent (PD) at 'The First Affiliated Hospital of Anhui Medical University teaching Hospital during the period of December 2008 to December 2015 was done. A two-layered duct-to-mucosa pancreaticojejunostomy over an internal transanastomotic stent was performed in all 65 patients.

**Results:** The in-hospital morbidity and mortality rate in the study was 47.6% and 1.5%, respectively. One patient died as a consequence of mesenteric ischemia. Pancreatic fistula occurred in one patient (1.5%) and was treated conservatively with good results. The wound infection was the most common surgical complication (13/65; 20%) and occurred more often in patients who had a biliary stent inserted endoscopically prior to surgery (10/24; 41.7%), as compared to those without the stent (3/41; 7.3%;  $P < 0.0001$ ).

**Conclusions:** The consequences of the present study recommend that a two-layered conduit to-mucosa pancreaticojejunostomy with inside trananastomotic stent is a sheltered anastomosis, connected with an okay of pancreatic fistula. The nearness of a biliary stent at the season of surgery speaks to a danger element for the improvement of postoperative injury contamination. In our information we have an aggregate number of 65 patients some of them we did endoscopy and some of them didn't. 24 patients were done endoscopy and in these cases 10 patients get wound contamination while 41 of our patients did not get endoscopy but rather 3 patients get wound disease. The summary of information is that the rate of wound contamination is high with patients is who get the endoscopy.

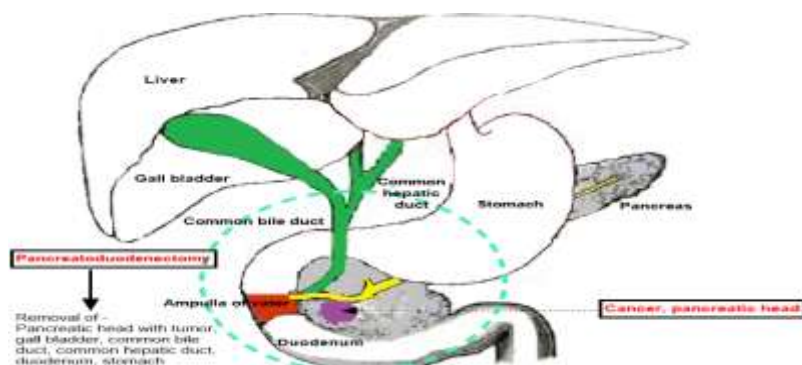
**Keywords:** Pancreatoduodenectomy, duct-to-duct (DTD) Pancreatic fistula, Pancreaticojejunostomy.

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### I. Introduction

Pancreatoduodenectomy (PD) is a method that employs major surgical strategy that includes both the pancreas and duodenum. This operation is typically performed to treat carcinogenic tumors on the head of the pancreas, malignant tumors of the bile duct, duodenal papilla, or duodenum that lies in close proximity to the pancreas and in some instances of pancreatitis. PD is a major procedure that demands surgical competency and a specialized care<sup>1,2,3,4,5</sup>. The chief reason that makes this procedure hypercritical is the occurrence of pancreatic fistula during pancreatic anastomosis creation. It has been found that even in standard specialized critical specialties the occurrence of pancreatic fistula ranges from 0-2%<sup>3,6,7,8</sup> to more than 20% in some cases<sup>9,10,11,12</sup>. Besides this dreaded complication that adds to significant morbidity and mortality, the anastomosis reconstruction procedure may lead to local abscess formation, sepsis, delayed gastric emptying and postoperative intra-stomach bleeding due to autolytic activity of the pancreatic juice<sup>1,2,3,4,5</sup>.

Basically during PD as shown in Figure 1, the common hepatic duct, the common bile duct along with the gall bladder, the cancerous pancreatic head as well as the encroached duodenum is excised. A direct anastomosis between the remaining pancreatic remnant and the jejunum is made.



**Figure1:** Demonstrates the classical pancreatoduodenectomy commonly known by Whipple’s procedure where removal of pancreatic head with tumor, common hepatic duct, common bile duct with the gall bladder and the encroached duodenum is performed followed by anastomotic apposition of pancreatic remnant and jejunum is performed.

Different centers deploy various methods of pancreatic anastomosis and there is no single consensus as to the best possible approach and strategy<sup>13,14, 15</sup>. Simple classical pancreaticojejunostomy have been the most widely well-known approach that comprises of either invagination technique or duct to mucosa pancreaticojejunostomy. These procedures further, may or may not deploy a stent between the anastomosis. In this study, we report our experience with the use of the classical procedure by creating an anastomosis in a single layered duct to mucosa pancreaticojejunostomy and highlight its consequences in terms of mortality and occurrence of pancreatic fistula.

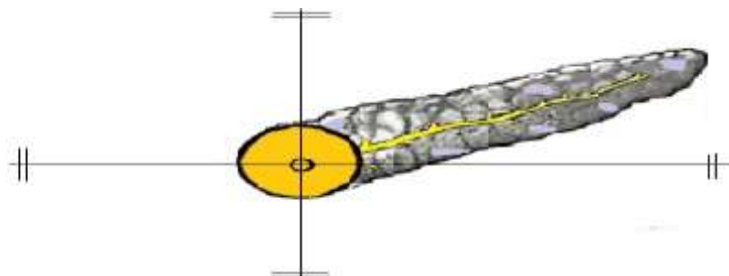
## II. Methods

### **Data collection:**

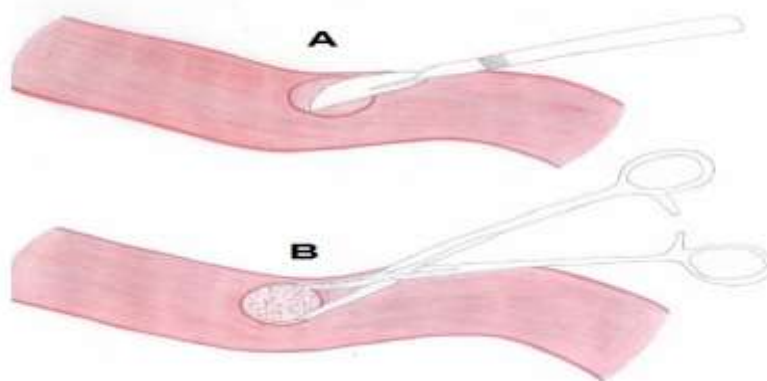
A retrospective study was conducted in all 65 patients that underwent pancreatoduodenectomy at the department of Hepatobiliary & Pancreatic Surgery, and Liver Transplantation between the periods of January 2008 and December 2015. All the records were extracted from the hospital database as well as from follow up clinics. The pre-operative parameters that were considered for analysis included– patient demographics, co-morbidities, history of current illness, past illness, laboratory data and imaging data. The patients that underwent diagnostic computed tomography were only considered for the surgery. Similarly, the evaluation of operability was done by endoscopic ultrasound as well as endoscopic retrograde Cholangiopancreatography in selected cases.

### **The surgery:**

The surgical procedure was performed by four PD specialists. The classical Whipple’s technique was employed for the anastomosis construction. Firstly, the proximal jejunum was brought from behind the colon to the right half of the middle colic vessels. Then, modified Cattell’s pancreaticojejunostomy<sup>16</sup> was performed first and the most proximal part of the loop in an end to side manner in two layers. For these procedures, absorbable monofilament polydioxanone sutures (Johnson&Johnson ; USA) with atraumatic needles were used. The procedure utilized is depicted in figure 2 where the back wall of the pancreatic remnant was dissected off the splenic vein as well as from the retro peritoneum for a distance of around 2cm from its cut edge.



**Figure 2:** This was followed by application of four 6/0 double armed interrupted sutures on the pancreatic duct at 3, 6, 9 and 12 o'clock position before starting the anastomosis procedure. These sutures were placed in an inside-out manner and if the pancreatic duct caliber was small then loupe magnification (2.5x) was performed. This was followed by seromyotomy of the back of the jejunum using the back side of the scalpel (Figure 3A) and the mucosa was removed off the seromucosal layer by the use of fine forceps (Figure3B) for the necessary space that the pancreatic stump remnant would occupy in the anastomosis; Finally, the outermost layers of the anastomosis were apposed by means of a running suture in an inside-out manner on the side of the pancreatic stump, taking enough pancreatic tissue from the pancreatic stump (Figure 3).

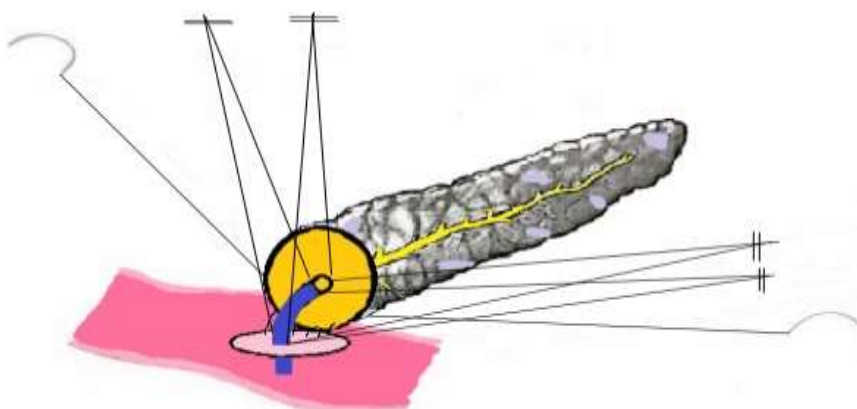


**Figure 3:** Demonstrated the method employed in creating an opening in the jejunum. Figure A shows blunt dissection by the back side of the scalpel while figure B shows the use of fine forceps.

**Anastomosis details:**

Firstly external anastomosis was created by connecting the posterior walls of the external layer of the divided pancreatic neck and the seromuscular layer of jejunum using a 4/0 running suture (Johnson and Johnson). It was made sure that the pancreatic duct was excluded from the suture line by placing a stent into the duct. The size of the stent (4-10Fr) to be inserted into the pancreatic duct was same as the internal diameter of the pancreatic duct extent and accordingly an aperture (1-2mm) was created into the jejunum. This was followed by duct to mucosa anastomosis between the main pancreatic duct and the jejunal mucosa with four interrupted 6-0 sutures over the inner trans-anastomotic stent.

The length of the stent used was about 8-10cm and it was inserted half into the main pancreatic duct and half into the jejunum. The stent was supported by one of the sutures of the pancreatic duct and the sutures closed after all the sutures participating in the anastomosis were tied down. The knots were placed externally in relation to the anastomosis. This was followed by performing anastomosis between the anterior walls of the divided pancreatic neck and the jejunum with the help of abundant bites of 4/0 running sutures (Figure 4).



**Figure 4:**

Care was always taken to avoid inadvertent pulling of the holding suture by the assisting surgeon so as to avoid laceration and cutting of the freshly sewn pancreatic remnant tissues. Following this procedure, two drains with negative suction were placed in the pancreatic anastomotic territory as well as nasogastric tube in the stomach. For the purpose of enteral feeding, a needle-catheter feeding jejunostomy was placed in all patients.

Post procedure, the patients received standard post-operative care. This comprised of continuation of antibiotics for 24 hours, proton pump inhibitors, and also subcutaneous octreotide 3x100µg every day for 7 days and low molecular weight heparin until the patients were discharged. The NG tube was taken out the next day or later if the amount of drainage was less than 500mL/day. The patients were allowed to drink water at day 6 of surgery while enteral feeding was continued up to the 7<sup>th</sup>. Post-operative day with progressively introducing pancreatic (low fat) diet as tolerated. The abdominal drains were checked regularly and specifically for the amylase content during the 2<sup>nd</sup> and 5<sup>th</sup> post-operative day to detect formation of pancreatic fistula. The pancreatic fistula was diagnosed if the drain, however small the content be, contained amylase that was three times the value of plasma amylase levels after the third post-operative day<sup>17,18</sup>. Similarly, if the amylase content in the drain was less or if

the drain had fluid volume less than 100ml, then the drain was removed on the fourth postoperative day. Likewise, delayed gastric emptying was diagnosed if the stomach aspirate contained fluid volume of more than 500mL/day for  $\geq 10$  days of surgery or if the patient could not take in normal food or persistent vomiting requiring NG tube reinsertion by 14<sup>th</sup> post-operative day<sup>19, 20</sup>.

The overall complications were evaluated by 5-grading scale proposed by De Oliveira et al<sup>21</sup> that is depicted in table 1. The mortality incorporated every single death that occurred within the 30 days of procedure including hospital deaths.

**Table 1:** shows the standard grading scale proposed and widely used by surgeons worldwide regarding post-operative grading of complications following PD procedure.

Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parental nutrition are also included
III	Requiring surgical, endoscopic or radiological intervention
IIIA	Intervention not under general anesthesia
IIIB	Interventions under general anesthesia
IV	Life- threatening complication (including CNS complications)* requiring IC/ICU management
IVA	Single organ dysfunction
IVB	Multiorgan dysfunction
V	Death of patient
Suffix 'd'	If the patient suffers from a complication at the time of discharge, the suffix 'd' (for disability) is added to the respective grade of complication. This label indicates the need for a follow up to fully evaluate the complication.
*Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks. CNS, central nervous system, IC –intermediate care, ICU- intensive care unit.	

**Statistical Analysis**

All the collected data’s were tabulated and were subjected to rigorous statistical analysis. The statistical method used was Yates correction and Fisher tests applying the SPSS (version -16, Chicago, USA) program. The p-value <0.05 was considered as statistical significant. The graphs and figures were constructed by graph pad prism and paintbrush.

**III. Results**

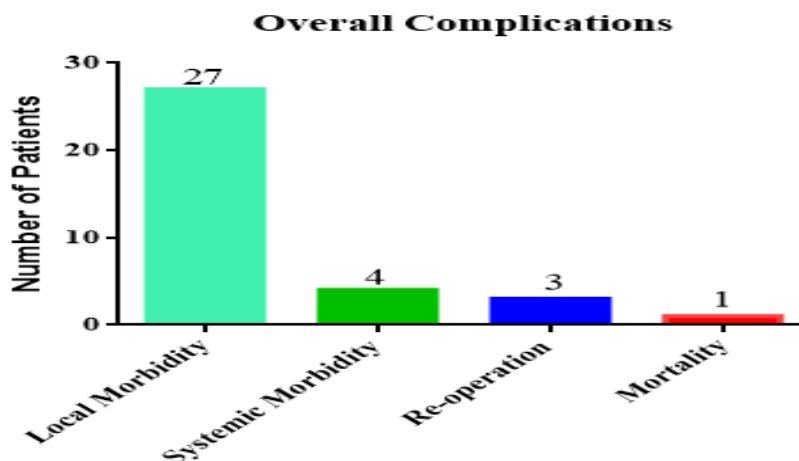
A total of 65 patients underwent PD out of which 39 were male and 26 were female patients and the mean age of the patients were 60 (range 45-76) years and most were 60% (39/65) were men. The surgical indications considered for the procedure are outlined in table 2. Preoperative endoscopic biliary stenting was doing in 24 patients.

**Table 2.** Patient characteristics

Age* (years)	60.8 (45-76)
Male/Female	39/26
Histological diagnosis	
<b>Malignant tumor</b>	55
Pancreatic head cancer	41
Distal bile duct cancer	2
Ampullary cancer	8
Metastasis to the pancreas	1
Other	3
<b>Benign tumor</b>	10
Chronic pancreatitis	7
Cystadenoma	1
Ampullary adenoma	2
*data expressed as median (range).	

It was observed that the occurrence of post-operative complications was in 47.6% of patients (31/65) out of which 41.5% and 6.1% was local and systemic complications respectively (Table2). When the complications were categorized into standard grading system (Table 1), it was found that the patients had major complications in 5% ( $\geq$  grade 3) that required surgical treatment (n=2) or ICU management (n=1). Similarly, two patients (3%) had to undergo reoperation as one of them developed intra-abdominal hemorrhage while the other had mesenteric ischemia. The latter patient had to be admitted to the ICU too due to development of multi-organ

failure due to development of pancreatitis of the remnant pancreas. The median length of hospital stay was 25 (territory 13-47) days.



Local complication in the form of intra-abdominal hemorrhage was observed in 2 patients on day 2 and day 5. These patients were urgently taken to the OT and urgent re-laparotomy was performed followed by ligation of mesenteric roots that were the source of bleeding. Moreover, one of the patients developed biliary leakage after the procedure at day 6 and again after 1 day of performing re-laparotomy. This patient was placed with an abdominal drain until no fluid drained out that was for about 29 after which the drain was taken out. Unfortunately, the patient developed tight biliary stricture at the anastomosis site at 12 months and is still in continuous follow up and is being treated with percutaneous trans-hepatic biliary drainage procedure. He is well till now. He still has the trans-anastomotic biliary channel at 30 month of follow up.

Among the local complications, wound infection was most common that occurred in 20% (13/65) of the cases. 41.7% of these patients (10/24) had endoscopically implanted biliary stent preceding surgery while 7.3% of the patients (3/41) did not have biliary stents before surgery ( $P < 0.0001$ ). Pathological reports obtained from the laboratory revealed that wound infection was chiefly caused by bacterial infections with *Escherichia coli* and *Enterococcus faecium* which were successfully treated with antibiotics.

Pancreatic anastomotic leakage was observed in 1 patient (1.5%) that remained asymptomatic and the diagnosis was only revealed in 3<sup>rd</sup> post-operative day when the drain fluid revealed significant higher levels of amylase. The patient was thus treated with continuous external drainage of the fluid, enteral feeding via feeding jejunostomy, intravenous antibiotics (piperacillin/tazobactam 4.5gm 3 times every day) and subcutaneous Octreotide (0.1mg 3 times day by day). This treatment was followed until there was no fluid in the drain, which was seen at 21st postoperative day. The absence of leakage was confirmed by a CT scan and the patient was discharged at 24 days of the surgery.

Similarly as depicted in Table 3, 4 patients suffered from systemic complications, where pneumonia predominated and some patients also developed MI and stroke. All of these patients were managed with standard medical that recovered.

There was 1 case of in hospital death that occurred as a result of major post-surgical complication, the patient died because of serious stomach sepsis as a result of extensive intestinal necrosis that developed at day 6 of surgery. This patient was diagnosed as a case of pancreatic head carcinoma, thus the superior mesenteric artery was dissected as the tumor mass had encroached the artery and reaching the border of tumor was mandatory. This patient died at day 9.

**Table 3.** Postoperative complications.

	Total number of patients N=65
Overall morbidity	31
<b>Local morbidity:</b>	27
Delayed gastric emptying	7
Wound infection	13
Intra-abdominal hemorrhage	2
Intestinal necrosis†	1
Cholangitis	1
Pancreatic fistula	1

Biliary fistula	1
Acute necrotizing pancreatitis	1
<b>Systemic morbidity:</b>	4
Pneumonia	2
Myocardial infection	1
Stroke	1
Re-operations	3
Mortality	1
Hospital stay(days)*	25(13-47)
*Data expressed as median (range). †Complications resulting in mortality	

#### IV. Discussion

Among commonly performed surgical procedures, PD is considered to be one of the most challenging procedures as it is associated with significant mortality and morbidity. It has been reported that even in specialized units, the occurrence of morbidity and mortality with this procedure is observed to be 40 - 60% and 0 - 5% respectively<sup>3,22,23,24</sup>. The occurrence of pancreatic fistula as the major complication carries the major bulk of complication and significant amount of in-hospital mortality while 20-40% postoperative deaths<sup>3, 9, 10, 11, 12, 22, 23, 24</sup>. Are contributed by other procedural complications like sepsis, peritonitis, abscess formation or intra-abdominal hemorrhage. Although there are many causes of pancreatic fistula formation, surgical causes or iatrogenic causes chiefly revolves around per procedural causes. The diseased pancreatic tissue is very fragile with soft texture and excising the tissue as well as suturing the tissue becomes difficult. Tying the knot around the pancreatic remnant primarily determines whether there will be any leakage or fistula in the future or not. The stability and viability of the knot still depends on the amount of texture and fatty infiltration on the gland which are the main risk factors for knot stability and development of pancreatic fistula<sup>25, 26, 27, 28, 29, 30</sup>. Besides, the delicate diseased pancreas may produce large amount of pancreatic juice compared to fibroses pancreas. This has been validated by studies that have demonstrated lower occurrence of anastomosis based complications in fibroses pancreatic tissue (chronic pancreatitis) compared to friable soft textured pancreatic tissue<sup>31</sup>. Thus numerous researches have aimed at finding a suitable agent or a suitable method to address this issue of anastomotic leakage and recently trans-pancreatic U-sutures have also been suggested so as to avoid or minimize tangential sheer forces during knot tying so as to avoid the extra stress in the tissue by the knot<sup>24, 32, 33</sup>. In this study, we observed that the occurrence of pancreatic anastomotic leakage after PD was significantly lower (1.5%) with modified duct to-mucosa pancreaticojejunostomy procedure. This finding of ours was in lieu with previous findings of some studies conducted earlier<sup>3,34,35</sup>. However, this finding was also contradictory with other studies that have found the reverse<sup>36,37,38</sup>. These lower rates of pancreatic anastomosis leaks have also been documented in both series that do and do not use pancreatic stents<sup>3,24,34</sup>. A noteworthy technique that they have deployed that differs from ours was that they constructed an external layer of the anastomosis with interrupted sutures and did not use pancreatic duct stent for duct to-mucosa anastomosis. Furthermore they also provided a buttress to the pancreatic stump by providing some horizontal mattress U-sutures in cases of soft and intermediate textured pancreas. The goal of these procedures was similar to our technique of incorporating the thick bites of thick pancreatic tissue so as to achieve a firm and tight anastomosis. Similarly the internal layer of duct to mucosa should be perfectly opposed to the wall so as to ensure undisturbed flow of pancreatic juice into the jejunum. The jejunum too be vigilantly so as to prevent cracks and crevices from where the pancreatic juice can leak out (Figure 2). The use of internal transanastomotic stent and loupe amplification can be particularly important in securing a tight anastomosis too.

Whether to use the pancreatic stent or not has received conflicting opinions but it is generally agreed in some studies that its use especially in cases of normal pancreatic duct and with normal textured pancreas, the use of stent is beneficial<sup>39,40, 41</sup>. Yet, as stated earlier, there are studies that have opined in contradiction to the use of pancreatic stent<sup>42,43,44</sup> making generalized opinion difficult. We in our study used the inner trans-anastomotic stent routinely in every one of our patients regardless of the status of the pancreatic duct or the pancreatic texture.

The in hospital mortality rate was 1.5% in our study, which is low as compared to other studies. Our study also revealed that the rate of post-operative wound infections were relatively higher (20%). This was specially observed in patients that had undergone biliary stenting prior to the procedure. This observation of ours has also been acknowledged in previous studies by different authors<sup>45, 46</sup>. This has led us to identify biliary stent in-situ as an important risk factor in the development of wound infection that would require further studies in the future.

## V. Conclusions

Based on our studies we can say that the utilization of two-layered duct to-mucosa pancreaticojejunostomy along with the trans anastomotic stent as a connecting channel between the pancreas and jejunum is the optimal method to avoid trans anastomotic leakage, pancreatic fistula formation and reduce the in- hospital complication rates. This process is safe and is associated with lower mortality. The practice of electively putting in biliary stent and PD performed with an intrinsic biliary stent is associated with higher chances of post-operative wound infection. Given the overall rarity of complications that require surgery familiarity with the published data and sound clinical judgment are key to successful patient outcomes.

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