Review Article

Pancreaticojejunostomy versus pancreaticogastrostomy after pancreaticoduodenectomy to prevent post-operative pancreatic fistula, a dissonance between evidence and practice

Abstract

Leakage of pancreatic enzymes leading to either formation of abdominal collection or pancreatic fistula is one of the most feared complications after pancreaticoduodenectomy. Owing to high morbidity and cost related to pancreatic fistula, multiple interventions including various types of pancreatic-enteric anastomosis have been proposed to prevent this complication. Despite some randomized controlled trials and meta-analyses favoring pancreaticogastrostomy over pancreaticojejunostomy, clinical practice has not witnessed any change in preference of individual surgeons. One of the underlying factors is that there are various ways of doing pancreatic anastomosis and trials have compared only specific techniques while a few novel techniques that have been reported to have very low pancreatic fistula risk have never been compared in randomized controlled trials comparing pancreaticogastrostomy versus pancreaticojejunostomy. Moreover individual surgeons’ comfort and training also matters, and in many instances same results are not reproduced as reported for primary center where technique was developed. So though a good number of randomized controlled trials have been conducted to compare pancreaticogastrostomy with pancreaticojejunostomy, variations in techniques of performing anastomosis limit external validity as well as pooling the data for meta-analysis.

Furthermore subgroup of patients with soft pancreas, who are at high risk of pancreatic leak, should be looked at separately for potential benefit of type of pancreatic anastomosis.

Introduction

Pancreaticoduodenectomy (PD) remains the only curative option for resectable pancreatic head, ampullary, duodenal and distal common bile duct tumors. Despite improvements in post-operative care and advancement in surgical techniques, morbidity related to this operation remains very high. According to recent report by St-Germain AT et al. up to 74% of patients suffer from at least one complication related to this complex surgical procedure [1]. Leakage of pancreatic enzymes leading to either formation of abdominal collection or pancreatic fistula is one of the most feared complications. Incidence of post-operative pancreatic fistula (POPF) after PD is reported to be from 11% to 47.7% in various reports [2,3]. This wide variation in occurrence of POPF is partly due to variability in definition of fistula particularly in older studies. Criteria to label pancreatic fistula was standardized by international study group on pancreatic fistula (ISGPF) in 2005 [4].

Furthermore due to high morbidity and cost related to pancreatic fistula [5], multiple interventions have been investigated to prevent this complication [6]. These include pharmacological interventions such as role of peri-operative octreotides administration, adjuncts to surgical anastomosis such as stenting of anastomosis or use of sealants, surgical techniques and site of pancreatico-enteric anastomosis. Of these, comparison of pancreaticogastrostomy with pancreaticojejunostomy is the most studies area. To the best of our knowledge ten randomized controlled trials have been conducted to date to find out better site of performing pancreatic anastomosis. Three of these trials concluded that pancreaticogastrostomy is superior to pancreaticojejunostomy.
to prevent POPF [7–9], while others failed to detect any significant difference. Pooling of data in reported meta-analysis has also not been able to reach a definitive conclusion. Of the two most recent meta-analyses reported, one has concluded that pancreaticogastrostomy is superior to pancreaticojejunostomy to prevent POPF [10] while the other concludes that there is no statistically significant difference [11].

Other than site of pancreatic anastomosis, details of surgical technique employed for anastomosis and individual surgeon variations are the factors to be kept in mind while looking at evidence related to pancreatic fistula. Moreover surgical approach is altered in many instances of high risk features; its value in pancreatic anastomosis needs to be explored.

Available literature evidence

Before we look at available evidence on occurrence of post-operative pancreatic fistula (POPF) and methods to prevent it, definition of post-operative pancreatic fistula needs to be understood. Before 2005 there was no uniform definition of POPF and studies reporting POPF as outcome labeled POPF according to criteria used at their centers and this definition varied from center to center. So pooling of data from these studies or comparing results of various studies reported before 2005 is not meaningful. For standardization and uniform reporting of POPF to allow comparison across studies, international study group on pancreatic fistula (ISGPF) in 2005 agreed upon an objective and internationally acceptable definition [4]. According to this definition POPF was labeled if there was drain output of any measurable volume of fluid on or after postoperative day 3 with amylase content greater than 3 times the serum amylase activity. It was further categorized into three grades (grades A, B, C) according to clinical impact on patient’s hospital course. Later in 2016, international study group in pancreatic surgery (ISGPS) updated the definition and reclassified grade A pancreatic fistula as biochemical leak only as this had no impact on clinical management, so this was no longer referred to as true pancreatic fistula. While grade B and C pancreatic fistulae were grouped as clinically relevant post-operative pancreatic fistulae (CR-POPF) [12]. Studies conducted after 2005 to compare pancreaticogastrostomy with pancreaticojejunostomy have used these definitions to enable meaningful comparison.

To the best of our knowledge, there are ten randomized controlled trials conducted to date to compare pancreaticogastrostomy versus pancreaticojejunostomy. Three of these trials found that occurrence of pancreatic fistula was significantly lower in pancreaticogastrostomy group [7–9]. These trials had used definition proposed by ISGPF to define pancreatic fistula. There were three trials conducted before 2005 which used definitions as used at their respective centers. Meta-analyses conducted on these trials have reached at different results. A recent meta-analysis conducted by Qin et al., found statistically significantly less POPF in pancreaticogastrostomy group as compared to pancreaticojejunostomy group [10]. This meta-analysis included all studies irrespective of their definition of pancreatic fistula. Another meta-analysis by Crippa et al., failed to detect any difference in the two groups [11], but random-effect model was used to analyze the results as opposed to former meta-analysis. However there is no trial or meta-analysis published as yet that reported superiority of pancreaticojunostomy over pancreaticogastrostomy.

Differences in surgical techniques

Individual Surgeon Variations: There are several ways of doing pancreatic anastomosis and employing one way of doing anastomosis as opposed to the other depends upon comfort and training of operating surgeon in addition to other factors. Adopting and mastering another way of doing the same task when surgeon is comfortable with one way is not always easy and may not reproduce the same results as proposed by other surgeons. This is why same technique has different rates of pancreatic fistula reported from different centers [13].

Other than conventional technique, there are reported improvisations with promising results, but not all of these have been studied in randomized controlled trials comparing pancreaticogastrostomy with pancreaticojejunostomy.

Pancreaticojejunostomy:Conventionally pancreaticojejunostomy is performed as end to side, double layer, duct to mucosa anastomosis in which inner layer incorporates full thickness jejunal wall to pancreatic duct and outer layer as seromuscular jejunal stitch to pancreatic tissue. Reported leak rate after conventional technique is 6–22% [14]. Invagination of pancreatic tissue with or without duct to mucosa stitches has been studied with promising results. Invagination with duct to mucosa stitches is reported to have rate of CR-POPF as low as 3.3% [15]. Binding pancreaticojejunostomy as described by Peng et al incorporates destruction of 3 cm jejunal mucosa by applying 10% carbolic acid followed by rinsing with 75% alcohol and normal saline. After doing pancreaticojejunal anastomosis an absorbable ligature is looped around the jejunum, with the invaginated pancreas inside. Randomized controlled trial comparing binding pancreaticojejunostomy with conventional technique found significantly lower fistula rate for binding technique. It reported no pancreatic fistula in 106 patients randomized to binding technique group [16]. This technique is not compared to pancreaticojejunostomy in any of the randomized controlled trials. Moreover similar results could not be obtained for this technique at other centres. Maggiori et al., in their study reported no decrease in pancreatic fistula, rather risk of haemorrhage was increased [17].

Isolated loop pancreaticojejunostomy has also been compared with pancreaticogastrostomy in randomized controlled trial and no significant difference was found in pancreatic fistula rate [18].

Pancreaticogastrostomy: Conventionally pancreaticogastrostomy is performed as invaginated double layer anastomosis to posterior wall of stomach. Fernandez et al., reported doing pancreaticogastrostomy with gastric partition in which they made pancreaticogastric anastomosis to partitioned part of stomach. They compared it with conventional pancreaticojejunostomy in a randomized controlled trial and demonstrated that this technique was significantly superior to pancreaticojejunostomy in reducing pancreatic fistula risk [7].
It has been proposed that lack of enterokinase and acidic environment in stomach inactivates pancreatic enzymes, which along with good blood supply of stomach may have role to play in reducing risk of anastomotic leak [19]. While potential of anastomotic leak is reduced by pancreaticocystogastrostomy, long term exocrine and endocrine functions are compromised more in these patients as compared to those who underwent pancreaticojejunostomy [20]. Furthermore risk of digestive tract bleeding is also more after pancreaticocystogastrostomy, though management of GI bleed is easy via upper gastrointestinal endoscopy should bleeding occur [21].

Subgroup at high risk of leakage: In addition to post-operative care and surgical technique, certain patient and disease related factors predispose patients to high risk of POPF development [22]. Soft texture of pancreas is an established risk factor for POPF [23]. There are only a few randomized controlled trials that have been conducted on or have reported separate subgroup analysis for this select subgroup of patients. Bassi et al., reported on difference in fistula rate after pancreaticocystogastrostomy versus pancreaticojejunostomy for patients with soft pancreas [24]. Contrary to that, subgroup of patients with soft pancreas in randomized controlled trial by Topal et al., demonstrated that pancreaticocystogastrostomy was superior to pancreaticojejunostomy for post-operative pancreatic fistula [9]. There has been no meta-analysis to date to compare pancreaticocystogastrostomy versus pancreaticojejunostomy in patients with intra-operative soft texture of pancreas which needs to be addressed via pooled data analysis.

Conclusion

Though a good number of randomized controlled trials have been conducted to compare pancreaticocystogastrostomy versus pancreaticojejunostomy, variations in techniques of performing anastomosis limit external validity. Furthermore this issue of variability in surgical technique across randomized controlled trials should be taken care of before pooling the data for meta-analysis. Moreover subgroup of patients with soft pancreas who are at high risk of pancreatic leak, should be looked at separately for potential benefit of site of anastomosis. In addition to that, other than statistical evidence, to change practice where learning of a new skill is required, many other factors including training, learning curve and required facilities have to be accounted for.

References


