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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 the most feared complications after pancreaticoduodenectomy. Owing to high morbidity and cost related to pancreatic fistula, multiple interventions including various types of pancreatico-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 facts 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 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 studied 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 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 ran-

dom 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 pancreaticojejunostomy 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 pancreaticogastrostomy, 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 pancreaticogastrostomy, 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 pancreaticogastrostomy 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 pancreaticogastrostomy was superior to pancreaticojejunostomy for post-operative pancreatic fistula [9]. There has been no meta-analysis to date to compare pancreaticogastrostomy 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 pancreaticogastrostomy 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

1. St-Germain AT, Devitt KS, Kagedan DJ, Barretto B, Tung S, et al. (2017) The impact of a clinical pathway on patient postoperative recovery following pancreaticoduodenectomy. *HPB*. [Link: https://goo.gl/Tb5K9w](https://goo.gl/Tb5K9w)
2. Yeo CJ, Cameron JL, Maher MM, Sauter PK, Zahurak ML, et al. (1995) A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Annals of surgery* 222: 580. [Link: https://goo.gl/5H7hHU](https://goo.gl/5H7hHU)
3. Aumont O, Dupré A, Abjean A, Pereira B, Veziant J, et al. (2017) Does intraoperative closed-suction drainage influence the rate of pancreatic fistula after pancreaticoduodenectomy?. *BMC surgery* 17: 58. [Link: https://goo.gl/czjvtj](https://goo.gl/czjvtj)
4. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, et al. (2005) International

Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 138: 8-13.

5. Williamsson C, Ansari D, Andersson R, Tingstedt B (2017) Postoperative pancreatic fistula-impact on outcome, hospital cost and effects of centralization. *HPB* 19: 436-442. [Link: https://goo.gl/NJyDw4](https://goo.gl/NJyDw4)
6. Lai EC, Lau SH, Lau WY (2009) Measures to prevent pancreatic fistula after pancreatoduodenectomy: a comprehensive review. *Archives of Surgery* 144: 1074-1080. [Link: https://goo.gl/2wFe1s](https://goo.gl/2wFe1s)
7. Fernández-Cruz L, Cosa R, Blanco L, López-Boado MA, Astudillo E (2008) Pancreatogastrostomy with gastric partition after pylorus-preserving pancreatoduodenectomy versus conventional pancreaticojejunostomy: a prospective randomized study. *Annals of surgery* 248: 930-938. [Link: https://goo.gl/ooNQMQ](https://goo.gl/ooNQMQ)
8. Figueras J, Sabater L, Planellas P, Munoz Forner E, Lopez Ben S, et al. (2013) Randomized clinical trial of pancreaticogastrostomy versus pancreaticojejunostomy on the rate and severity of pancreatic fistula after pancreaticoduodenectomy. *British Journal of Surgery* 100: 1597-1605. [Link: https://goo.gl/mHaHKh](https://goo.gl/mHaHKh)
9. Topal B, Fieuws S, Aerts R, Weerts J, Feryn T, et al. (2013). Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. *The Lancet Oncology* 14: 655-662. [Link: https://goo.gl/G1RC3d](https://goo.gl/G1RC3d)
10. Qin H, Luo L, Zhu Z, Huang J (2016) Pancreaticogastrostomy has advantages over pancreaticojejunostomy on pancreatic fistula after pancreaticoduodenectomy. A meta-analysis of randomized controlled trials. *International Journal of Surgery* 36: 18-24. [Link: https://goo.gl/8kb2Eo](https://goo.gl/8kb2Eo)
11. Crippa S, Cirocchi R, Randolph J, Partelli S, Belfiori G, et al. (2016). Pancreaticojejunostomy is comparable to pancreaticogastrostomy after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. *Langenbeck's Archives of Surgery* 401: 427-437. [Link: https://goo.gl/8kb2Eo](https://goo.gl/8kb2Eo)
12. Bassi C, Marchegiani G, Dervenis C, Sarr M, Hilal MA, et al. (2016). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery*. [Link: https://goo.gl/Ejoh5u](https://goo.gl/Ejoh5u)
13. Gouma DJ, Van Geenen RC, van Gulik TM, de Haan RJ, de Wit LT, et al. (2000). Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. *Annals of surgery* 2:786. [Link: https://goo.gl/r1Wh7F](https://goo.gl/r1Wh7F)
14. Motoi F, Egawa S, Rikiyama T, Katayose Y, Unno M (2012) Randomized clinical trial of external stent drainage of the pancreatic duct to reduce postoperative pancreatic fistula after pancreaticojejunostomy. *British Journal of Surgery* 99: 524-531. [Link: https://goo.gl/74jxj3](https://goo.gl/74jxj3)
15. Zhu B, Geng L, Ma YG, Zhang YJ, Wu MC (2011) Combined invagination and duct-to-mucosa techniques with modifications: a new method of pancreaticojejunal anastomosis. *Hepatobiliary & Pancreatic Diseases International* 10: 422-427. [Link: https://goo.gl/ymTPRA](https://goo.gl/ymTPRA)
16. Peng SY, Wang JW, Lau WY, Cai XJ, Mou YP, et al. (2007). Conventional versus binding pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized trial. *Annals of surgery* 245: 692. [Link: https://goo.gl/mTTtor](https://goo.gl/mTTtor)
17. Maggiori L, Sauvanet A, Nagarajan G, Dokmak S, Aussilhou B, et al. (2010). Binding versus conventional pancreaticojejunostomy after pancreaticoduodenectomy: a case-matched study. *Journal of Gastrointestinal Surgery* 14: 1395-1400. [Link: https://goo.gl/JS9kgv](https://goo.gl/JS9kgv)
18. El Nakeeb A, Hamdy E, Sultan AM, Salah T, Askr W, et al. (2014). Isolated Roux loop pancreaticojejunostomy versus pancreaticogastrostomy after pancreaticoduodenectomy: a prospective randomized study. *HPB* 16: 713-722. [Link: https://goo.gl/rQp3mD](https://goo.gl/rQp3mD)

19. Oneil Machado N (2012) Pancreatic fistula after pancreatectomy: definitions, risk factors, preventive measures, and management—review. *International journal of surgical oncology*. [Link: https://goo.gl/ji3QiH](https://goo.gl/ji3QiH)
20. Roeyen G, Jansen M, Ruysinck L, Chapelle T, Vanlander A, et al. (2016). Pancreatic exocrine insufficiency after pancreaticoduodenectomy is more prevalent with pancreaticogastrostomy than with pancreaticojejunostomy. A retrospective multicentre observational cohort study. *HPB* 18: 1017-1022. [Link: https://goo.gl/YxEuRq](https://goo.gl/YxEuRq)
21. Clerveus M, Morandeira-Rivas A, Picazo-Yeste J, Moreno-Sanz C (2014) Pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy: a systematic review and meta-analysis of randomized controlled trials. *Journal of Gastrointestinal Surgery* 18: 1693-1704. [Link: https://goo.gl/uS52ee](https://goo.gl/uS52ee)
22. Soreide K, Labori KJ (2016) Risk factors and preventive strategies for post-operative pancreatic fistula after pancreatic surgery: a comprehensive review. *Scandinavian journal of gastroenterology* 51: 1147-1154. [Link: https://goo.gl/txbCfT](https://goo.gl/txbCfT)
23. Yang MW, Deng Y, Huang T, Zhang LD (2017) Clinical study on the relationship between pancreatic fistula and the degree of pancreatic fibrosis after pancreatic and duodenal resection. *Zhonghua wai ke za zhi [Chinese journal of surgery]*. 55: 373. [Link: https://goo.gl/PGnB6b](https://goo.gl/PGnB6b)
24. Bassi C, Falconi M, Molinari E, Salvia R, Butturini G, et al. (2005). Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. *Annals of surgery* 242: 767-773. [Link: https://goo.gl/hBda7J](https://goo.gl/hBda7J)