Invaginated Duct to Mucosa Pancreaticojejunostomy Reduced Pstoperative Pancreatic Leakage: A Matched Case-Controlled Study

Guo-Liang Yao
The First Hospital Affilated to Henan University of Science and Technology
Meng-Jiao AN
The First Hospital Affiliated to Henan University of Science and Technology
YongGang Fan (fyg196809@qq.com)
The First Hospital Affiliated to Henan University of Science and Technolgoy

Research

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Abstract

Background Postoperative pancreatic leakage was also the obstacle of pancreaticoduodenectomy (PD) which always followed the failure of pancreaticojejunostomy. Dozens of pancreaticojejunostomy had been reported. None showed superiority over others. To assess the potential advantages of invaginated duct to mucosa pancreaticojejunostomy (invaginated D-M PJ), we introduced this study.

Methods Retrospectively analyzed the related data from the patients who had their pancreaticodedunostomy due to malignant tumor in The First Affiliated Hospital to Henan University of Science and Technology during January 2017 to August 2019. According to the different procedure of pancreaticojejunostomy, the patients divided into custom D-M group and invaginated D-M group. Sex, age, pancreatic duct size and pancreatic texture were matched. Pancreatic leakage and other complications were compared. SPSS 16.0 was employed for analysis.

Results 48 pairs of patients were involved. Both groups had almost the same baseline characterisitics, such as Sex (P=1.000), Age (P=0.897), ASA (P=0.575), BMI (P=0.873), pancreatic duct size (P=0.932), pancreatic texture (P=1.000) and tumor origin (P=0.686). No statistical difference was observed relation to operation outcomes, such as operation time (P=0.632), pancreaticojejunostomy time (P=0.748), blood loss (P=0.617) and number of required transfusion (P=0.523). Pancreatic leakage was significantly declined for invaginated D-M group (P=0.005). The difference of other complications, such as, bleeding (P=0.617), biliary leakage (P=0.646), pneumonia (P=0.594) and thrombosis (P=0.714), didn't reach statistical significance. Postoperative hospitalization was almost the same for both groups (P=0.764).

Conclusions Invaginated D-M PJ could reduce pancreatic leakage followed PD. Invaginated D-M PJ should be a choice for the patients who had PD.

Background

Pancreaticodudenectomy(PD) was one of the most problematic operations with high morbidity and mortality [1–4]. Most mortality was associated to pancreatic leakage which was mainly secondary to the failure of pancreaticojejunostomy (PJ). Dozens of anastomosises had been introduced; pancreatic leakage was still the obstacle of PD. Duct to mucosa (D-M) anastomosis and its modifications might be the most popular ones, while, none was the standard. Kakita anastomosis [5] and Blumgart anastomosis [6] were the most widely used procedures with lower pancreatic leakage. Hong's single stitch anastomosis [7] was also popular in china. None showed the significant superiority over others [8]. As to the pancreaticojejunostomy, invaginated procedure was still popular since its introduction. Chen's U-suture PJ [9] and Peng's binding PJ [10, 11] were still widely used. No consensus of the method of PJ was reached jet [12, 13]. All the procedures in used now had some advantages, while disadvantages still existed. That was partially the reasons why none procedure of PJ was shown the superiority over others. Now, we practiced a novel procedure of PJ which theoretically involved all the advantages mentioned before. That is invaginated D-M PJ.

Materials And Methods

Patients characteristic

All the patients administrated in The First Affiliated Hospital to Henan University of Science and Technology during January 2017 to August 2019 who needed PD for malignant tumor. All the operations were completed by the same team. This was a retrospectively designed trial. This clinical trial was approved by the ethics committee of The First Affiliated Hospital to Henan University of Science and Technology.

According to the procedure of PJ, we divide the patients into two groups: Custom D-M group and invaginated D-M group. All patients included were aged 18 to 80 years old; the American society of anesthesiologists (ASA) classification should be at 1 to 3; the diagnosis was approved by pathology; enhanced CT scan and MRCP were routinely performed. All patients included should be proved by enhanced CT or / and enhanced MR of no tumor invasion of vessels. All pancreatic duct size was dilated more than 2 mm. In case of bias control, we matched some factors. The matched factors were age (± 5 y), sex, pancreatic texture and pancreatic duct size (± 1 mm). Those factors were reported as important risk factors of pancreatic leakage[9]. All the characteristics of the two groups were list in the Table 1.

Table 1
, Characteristics of included patients

	Custom D-M (48)	Invaginated D-M (48)	P
Sex (M/F)	20/28	20/28	1.000
Age	61.7 ± 11.2	63.3 ± 10.5	0.897
ASA			0.575
□	5	7	
□	26	21	
□	17	20	
BMI (Kg/m^2)	24.8 ± 5.3	23.1 ± 3.8	0.873
Pancreatic duct size (mm)	3.1 ± 1.0	3.4 ± 1.2	0.932
Pancreatic texture			1.000
Firm	38	38	
soft	10	10	
Tumor origin			0.686
Biliary duct	18	15	
Pancreas	13	11	
Duodenum	6	10	
Ampulla	11	12	
ASA: American society of Anesthesiologists classification			

Operation procedure

All the operations were performed under general anesthesia. Pancreaticoduodenectomy was performed with local lymph nodes dissection. Jejunal limb was brought up through retrocolic root. After end to side PJ, cholangiojejunostomy was performed with 4 – 0 knotless suture (Stratafix, Ethicon) by a running suture about 8 cm distal to the PJ. Gastrojejunostomy was performed by a circular stapler (Panther) about 50 cm distal to cholangiojejunostomy. Additional jejunojejunostomy was performed by 4 – 0 knotless suture (Stratafix, Ethicon) about 10 cm distal to gastrojejunostomy. The difference between the two groups was the procedure of PJ. Custom D-M group was performed as modified Blumgart anastomoses descript by Shoji Kawakatsu [8]. Invaginated D-M group was performed as follow: a 3 – 0 polypropylene suture (Prolene, Ethicon) was employed to finish the anastomosis. The first stitch transfixed pancreas from anterior to posterior at about 1 cm from the superior board of pancreatic neck where located 1.5 cm distal to the pancreatic cutting end. The needle gone through the seromuscular of

the jejunum limb at the antimesenteric margin. Then, the first knot was made anteriorily shown as Fig. 1. The second stitch was about 1 cm departed from the first knot which was also 1.5 cm distal to the pancreatic cutting end. The second stitch transfixed the pancreatic neck from anterior to posterior (Fig. 2), then, it gone through the seromuscular layer of the jejunum 1 cm from the first stitch (Fig. 2). The needle gone through the pancreas from posterior to anterior about 1 cm distal to the pancreatic cutting end (Fig. 2), then, it gone through the seromuscular layer of the jejunum 1 cm from the first knot (Fig. 2). The suture was strengthened, and duplicated the second suture (Fig. 2). When the suture reached to the superior of pancreatic duct, it suspended. Then, duct to mucosa anastomosis was performed as custom D-M by 4 – 0 polyglactin suture (Vicryl Plus, Ethicon). After duct to mucosa anastomosis, pancreaticojejunostomy continued as descript above until to the inferior board of pancreatic neck. The last stitch was just like the first one. When the needle gone through the pancreatic neck about 1.5 cm distal to the pancreatic cutting end from anterior to posterior, it gone through the seromuscular layer of the jejunum limb; then, the second knot was made (Fig. 3). Before making the knot, what was emphasized was to strengthen every stitch moderately. Others should be emphasized were following: the jejunal serosa was destructed by electrocoagulation to accelerate healing of pancreatic cutting end and jejunum limb as descript by Hong [7]; pancreatic duct stent should be placed when duct to mucosa anastomosis; pancreatic duct should be separated about 2 mm when transaction of pancreas, this separation facilitated the invigation of pancreatic duct to mucosa of jejunum. Drainage tubes should be placed around cholangiojejunostomy and pancreaticojejunostomy with additional pelvic drainage when necessary. Peritoneal lavage with distilled water was emphasized before abdominal closure.

Perioperative management

Percutaneous transhepatic cholangial drainage (PTCD) were perform when cholangitis existed. Anemia correction should be performed routinely to 90 g/L or above. Serum albumin should be maintained at normal level. Breathing exercises were performed at least 2 days before operation. The pressure of O_2 and CO_2 should be at normal level by arterial blood gas analysis.

Postoperative management was performed according to the principle of Enhanced Recovery after Surgery (ERAS) [14]. Gastric tube was removed after operation when the patient recovered from anesthesia. Abdominal drainage amylase test was routinely performed at 1, 3, 7 day postoperatively with additional test when pancreatic leakage was suspected. Abdominal drainage tubes were removed when the drainage was less than 20 ml/d, which should be retained at least 7 days postoperatively. Abdominal CT scan was routinely performed to ensure no ascites before drainage removal. Discharged criteria was set as recovery to semifluid diet without symptomatic pancreatic leakage or biliary leakage at least 7 days postoperatively.

Definition

Primary endpoint was pancreatic leakage. Pancreatic leakage was detected following the International Study Group of Pancreatic Fistula (ISGPF) [15]. The severity of pancreatic leakage was classified

according to the criteria of ISGPF. Bleeding means hematochezia or haematemesis or blood drainage from abdominal cavity. Mortality was limited to 30 days postoperatively.

Statistical analysis

SPSS 16.0 was used to analyze the data. The measurement data, including age, BMI, pancreatic duct size, operation time, pancreaticojejunostomy time, blood loss, and postoperative hospitalization, were compared with t tests. The numerical data, such as sex, American Society of Anesthesiologists (ASA) classification, pancreas texture, tumor origin, number of required transfusion, pancreatic leakage, bleeding, biliary leakage, pneumonia, and thrombosis, were compared with chi square tests. $P < 0.05$ was considered to be significant.

Results

Finally, 48 pairs of patients were involved in this study. Both groups had parallel baseline characteristics (Table 1). Relation to the operative outcomes, both groups had almost the same operation time (224.6 ± 50.5 min VS. 209.8 ± 45.3 min; P = 0.632) and pancreaticojejunostomy time (15.3 ± 5.2 min VS. 13.8 ± 4.7 min; P = 0.748). No statistical difference was observed relation to blood loss (250.6 ± 33.7 ml VS. 280.1 ± 45.3 ml; P = 0.617) and the number of required transfusion (4/48 VS. 7/48; P = 0.523) (Table 2).

Table 2
, operative outcomes

	Custom D-M (48)	Invaginated D-M (48)	P
Operation time (min)	224.6 ± 50.5	209.8 ± 45.3	0.632
Pancreaticojejunostomy time (min)	15.3 ± 5.2	13.8 ± 4.7	0.748
Blood loss (ml)	250.6 ± 33.7	280.1 ± 45.3	0.617
Required transfusion	4	7	0.523

The primary endpoint was pancreatic leakage. Both groups had no grade C pancreatic leakage. A statistical difference was observed relation to grade A and grade B pancreatic leakage (15/48 VS. 4/48; P = 0.005). Further comparing shown the difference mainly came from decreased risk of grade B pancreatic leakage of invaginated D-M group (7/48 VS. 1/48; P = 0.027). 3 bleeding in custom D-M group including 1 intraabdominal bleeding, and 1 in invaginated D-M group were observed. Others complained hematochezia. The difference didn't reached statistical significance (P = 0.617). All the patients cured by conservative treatment. No re-operation was performed. 3 biliary leakages in custom D-M group and 2 in invaginated D-M group were observed, but this difference was not significant (P = 0.646). Pneumonia was another common complication. There was no statistical difference between the two groups (7/48 VS. 10/48; P = 0.594). Thrombosis was not rare in old patients postoperatively. 5 in custom D-M group and 3 in invaginated D-M group progressed lower limber venous thrombosis. The difference didn't reached

statistical significance (P = 0.714). No mortality was observed in both groups. No re-operation was performed. The postoperative hospitalization was almost the same for both groups (12.4 ± 3.1d VS. 13.3 ± 3.8d; P = 0.764) (Table 3).

Table 3
, postoperative outcomes

	Custom D-M (48)	Invaginated D-M (48)	P
Pancreatic leakage			0.005
Grade A	8	3	0.109
Grade B	7	1	0.027
Grade C	0	0	
Bleeding *	3	1	0.617
Biliary leakage	3	2	0.646
Pneumonia	7	10	0.594
Thrombosis#	5	3	0.714
Mortality	0	0	
Re-operation	0	0	
Postoperative hospitalization (d)	12.4 ± 3.1	13.3 ± 3.8	0.764

*One in classical D-M group had intraabdominal bleeding who had transfusion; others had hematochezia. All of them recovered by conservative treatment.

#Represented as intermuscular venous thrombosis of lower extremity

Discussion

Pancreatic leakage was following the failure of the anastomosis of pancreatic stump. It was still the most fatal morbidity after pancreaticoduodenectomy (PD). Duct to mucosa pancreaticojejunostomy (PJ) might be the most popular method worldwide. Though a serial of modifications had been introduced [7–9], pancreatic leakage didn't decrease. Each modification had some advantages over others theoretically, while, defect still existed. Kakita duct to mucosa anastomosis [5] had penetrating sutures to close the pancreatic cutting end and the serosa of jejunum limb. This penetrating suture was prone to progress tangential shear following failure of anastomosis, which led to pancreatic leakage. Blumgart anastomosis [8, 16] adopt transpancreatic U-suture which avoided tangential shear and the pancreatic stump could be covered by jejunum serosa to protect the knots from cutting through the pancreatic tissue. This U-suture might cause ischemia of the pancreatic stump, which hampered the healing of duct to mucosa anastomosis, and increased the risk of pancreatic leakage from the pancreatic cutting end

followed by hemorrhage. Although the modified Blumgart anastomosis [8] adopted U-suture to avoid shear force, the pancreatic leakage was detected without any statistical difference. Maybe the potential ischemia of pancreatic stump offset the potential benefit from less tangential shear force. Hong's single stitch duct to mucosa PJ [7] had something like Kakita anastomosis. It was also prone to progress tangential shear of the pancreatic stump. It emphasized destruction of the jejunal serosa by electrocoagulation which might accelerate healing of pancreatic cutting end and jejunum limb. Chen's anastomosis was in fact an invagination PJ. Chen's U-suture was something different from Blumgart U-suture. Its shear force was parallel the vessels, this change greatly reduced the risk of ischemia of pancreatic stump. While, the pancreatic stump was invaginated into jejunum serosa by chen's U-suture, the seromuscular layer of jejunum could protect the pancreas from rupture by the suture. As invagination asastomosis, chen's anastomosis had a potential risk. Even one suture was failure, a big defect of the anastomosis formed which may lead to high volume of pancreatic leakage. That may be lethal. That was why we adopt D-M PJ recent years.

The invaginated D-M PJ anastomosis which we introduced was indeed a modification of custom D-M PJ. Duct to mucosa suture was performed as usual. What should be emphasized was the pancreatic duct stent implantation, this procedure may reduce the risk of pancreatic leakage potentially [17, 18], though controversy existed [19]. Four to six sutures might be suitable. Too many sutures might increase the risk of ischemia. Another thing should be emphasized was separation of pancreatic duct. 2 to 3 mm separation of pancreatic duct might facilitate the pancreatic duct invaginated into mucosa of jejunum, which might accelerate healing. The suturing of pancreatic stump and jejunum seromuscular was just like Chen's U-suture which ensured the pancreatic stump wholly invaginated into jejunal seromuscular. This procedure greatly decreased the tangential shear force of duct to mucosa anastomosis followed by decreased risk of pancreatic leakage. Our destruction by electrocoagulation of the jejunal serosa accelerated healing of pancreatic stump and jejunal serosa which also decreased the risk of pancreatic leakage. By our procedure, what should be emphasized was avoidance to suture through the pancreatic duct to reduce pancreatic leakage from pinhole. Another thing should be emphasized was the strengthening of every stitch moderately before the last knot when suturing pancreatic stump and jejunal serosa. As a running suture, potential time saving was obvious. Theoretically, the invaginated D-M PJ integrated all the advantages mentioned above without obvious defect, it reduced the risk of pancreatic leakage.

Our study showed no grade C pancreatic leakage in both groups. A decreased risk of grade B pancreatic leakage was observed by invaginated D-M PJ, which resulted in statistically decreased risk of whole pancreatic leakage. Other complications were the same between the two groups. This reality was just according to the theory above.

The limitation of this method was its adaptability. Not all the patients adapted this method. When the pancreatic duct didn't dilate, invaginated D-M PJ wasn't suitable. As a retrospectively designed trial, bias might exist. Although some risk factors were matched, those were not the all. The small volume might also lead to some bias.

Conclusions

Base on the limited practice, invaginated D-M PJ could reduce pancreatic leakage after PD. Invaginated D-M PJ should be a choice for the patients who had PD. A prospective trial should be planned to further assess its superiority.

Abbreviations

PD: pancreaticoduodenectomy; D-M PJ: duct to mucosa pancreaticojejunostomy; D-M: duct to mucosa anastomosis; PJ: pancreaticojejunostomy; ASA: American society of anesthesiologists classification; PTCD: Percutaneous transhepatic cholangial drainage; ERAS: Enhanced Recovery after Surgery; ISGPF: International Study Group of Pancreatic Fistula.

Declarations

Ethics approval and consent to participate

This trial was approved by the ethics committee of The First Affiliated Hospital to Henan University of Science and Technology. All the patients included had a written consent to participate to this trial.

Availability of data and material

All the data were included in this paper.

Competing interests

All the authors, including Yao Guo-Liang, An Meng-Jiao and Fan Yong-Gang, declared no competing interest.

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Authors' contributions

Fan Yong-Gang and Yao Guo-Liang completed all the operations and designed this trial. Yao Guo-Liang and An Meng-Jiao extracted and analyzed the data. Fan Yong-Gang explained the differences. Yao Guo-Liang, An Meng-Jiao and Fan Yong-Gang together wrote this article.

Consent for publication

All the authors, including Yao Guo-Liang, An Meng-Jiao and Fan Yong-Gang, approved to publish this article on Journal of Experimental and Clinical Cancer Research.

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References

1. Ke S, Ding XM, Gao J, et al. A prospective, randomized trial of Roux-en-Y reconstruction with isolated pancreatic drainage versus conventional loop reconstruction after pancreaticoduodenectomy. Surgery. 2013;153:743–52.
2. Topal B, Fieuws S, Aerts R, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. Lancet Oncol. 2013;14:655–62.
3. Kimura W, Miyata H, Gotoh M, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. Ann Surg. 2014;259:773–80.
4. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg. 2015;220:530–6.
5. Kakita A, Takahashi T, Yoshida M, et al. A simpler and more reliable technique of pancreatojejunal anastomosis. Surg Today. 1996;26:532–5.
6. Grobmyer SR, Kooby D, Blumgart LH, et al. Novel pancreaticojejunostomy with a low rate of anastomotic failure-related complications. J Am Coll Surg. 2010;210:54–9.
7. Hong DF, Liu YH, Zhang YH, et al. The role of Hong's single-stitch duct to mucosa pancreaticojejunostomy in laparoscopic pancreaticoduodenectomy. Zhonghua Wai Ke Za Zhi. 2017;55:136–40.
8. Kawakatsu S, Inoue Y, Mise Y, et al. Comparison of pancreatojejunostomy techniques in patients with a soft pancreas:Kakita anastomosis and Blumgart Anastomosis. BMC Surg. 2018;18:88.
9. Chen XP, Huang ZY, Lau JW, et al. Chen’s U-Suture Technique for End-to-End Invaginated Pancreaticojejunostomy Following Pancreaticoduodenectomy. Ann Surg Oncol. 2014;21:4336–41.
10. Buc E, Flamein R, Golffier C, et al. Peng's binding pancreaticojejunostomy after pancreaticoduodenectomy: a French prospective study. Am J Surg. 2002;183:283–5.
11. Peng SY, Wang JW, Lau WY, et al. Conventional versus binding pancreaticojejunostomy after pancreaticoduodenectomy. A prospective randomized trial. Ann Surg. 2007;245:692–8.
12. El Nakeeb A, El Hemaly M, Askr W, et al. Comparative study between duct to mucosa and invagination pancre- aticojejunostomy after pancreaticoduodenectomy: a prospective randomized study. Int J Surg. 2015;16:1–6.
13. Bai X, Zhang Q, Gao S, et al. Duct-to-mucosa vs invagi- nation for pancreaticojejunostomy after pancreaticoduodenectomy: a prospec- tive, randomized controlled trial from a single surgeon. J Am Coll Surg. 2016;222:10–8.
14. Morgan KA, Lancaster WP, Walters ML, et al. Enhanced recovery after surgery protocols are valuable in pancreas surgery patients. J Am Coll Surg. 2016;222:658–64.

15. International Study Group of Pancreatic Surgery (ISGPS). Pancreatic anastomosis after pancreatoduodenectomy: A position statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2017;161:1221–34.
16. Kleespies A, Rentsch M, Seeliger H, et al. Blumgart anastomosis for pancreaticojejunostomy minimizes severe complications after pancreatic head resection. Br J Surg. 2009;96:741–50.
17. Zhang Guo-qiang, Li X-H, Ye X-J, et al. Internal Versus External Drainage With aPancreatic Duct Stent For Pancreaticojejunostomy During Pancreaticoduodenectomy for Patients at High Risk for Pancreatic Fistula: A Comparative Study. Journal of surgical research. 2018;232:247–56.
18. Pessaux P, Sauvanet A, Mariette C, et al. External pancreatic duct stent decreases pancreatic fistula rate after pancreaticoduodenectomy: prospective multicenter randomized trial. Ann Surg. 2011;253:879–85.
19. Suzuki S, Kaji S, Koike N, et al. Pancreaticoduodenectomies with a duct-to-mucosa pancreaticojejunostomy anastomosis with and without a stenting tube showed no differences in long-term follow-up. J Hepatobiliary Pancreat Sci. 2011;18:258–62.

Figures

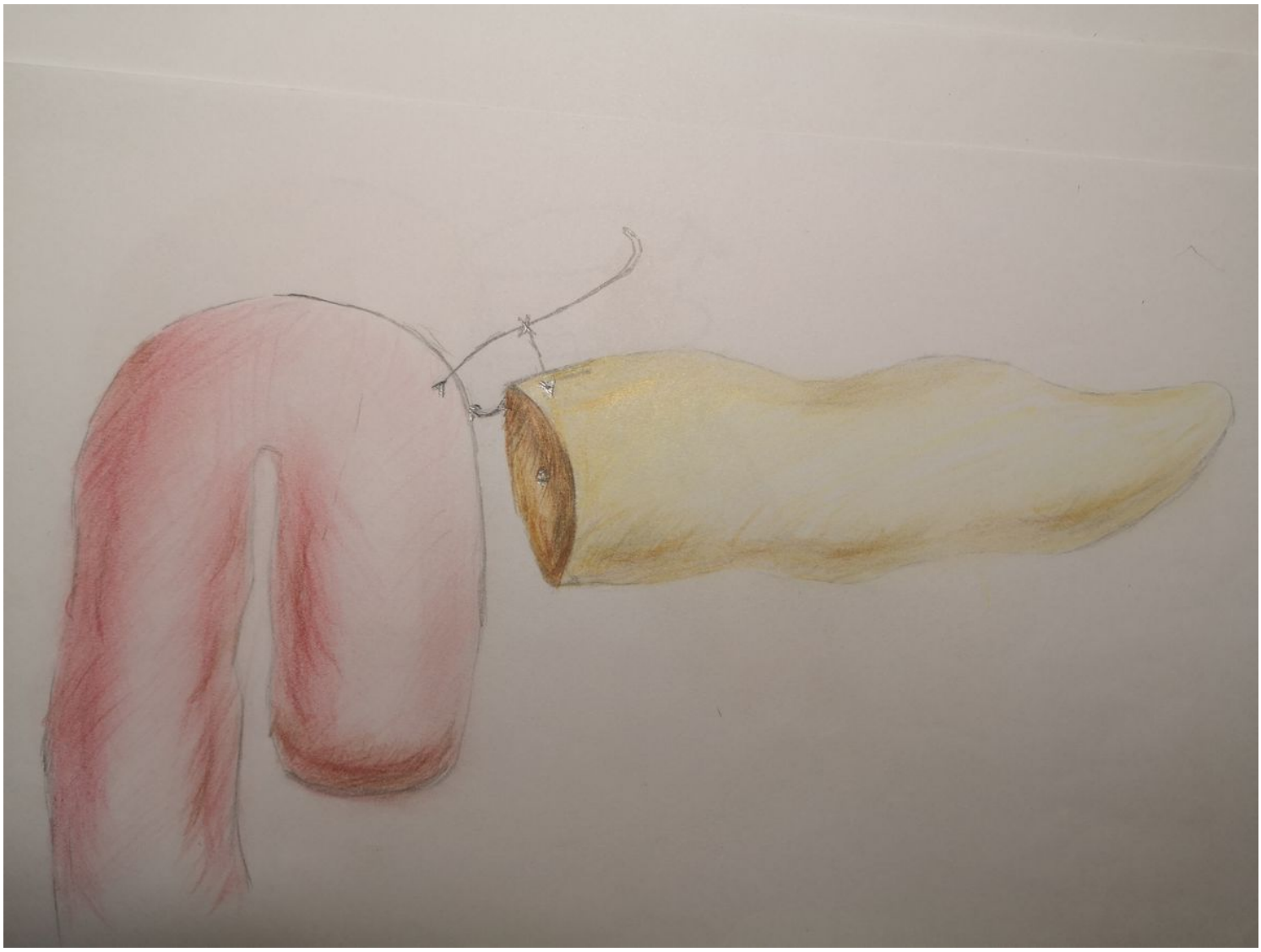

Figure 1

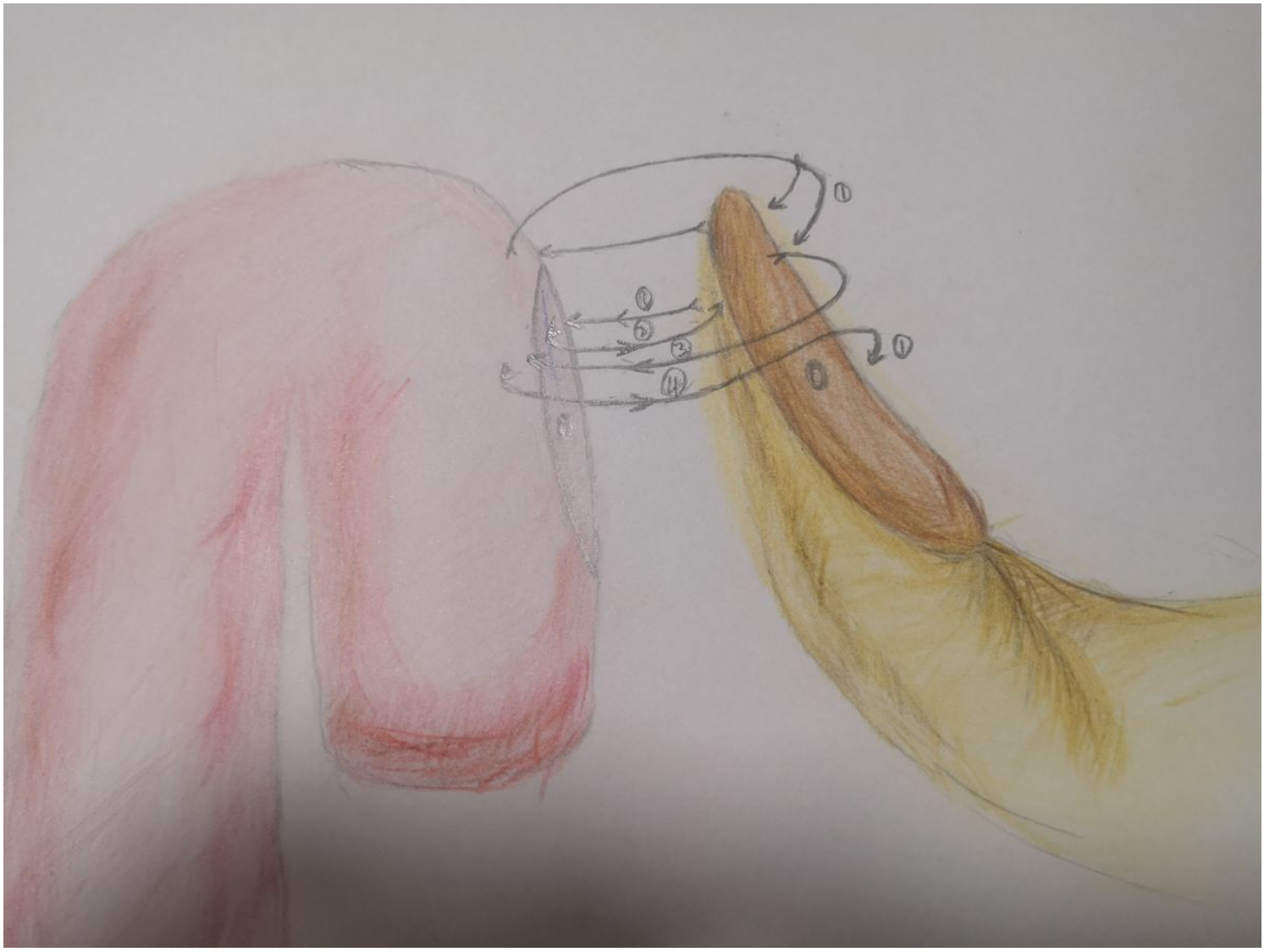

Figure 2

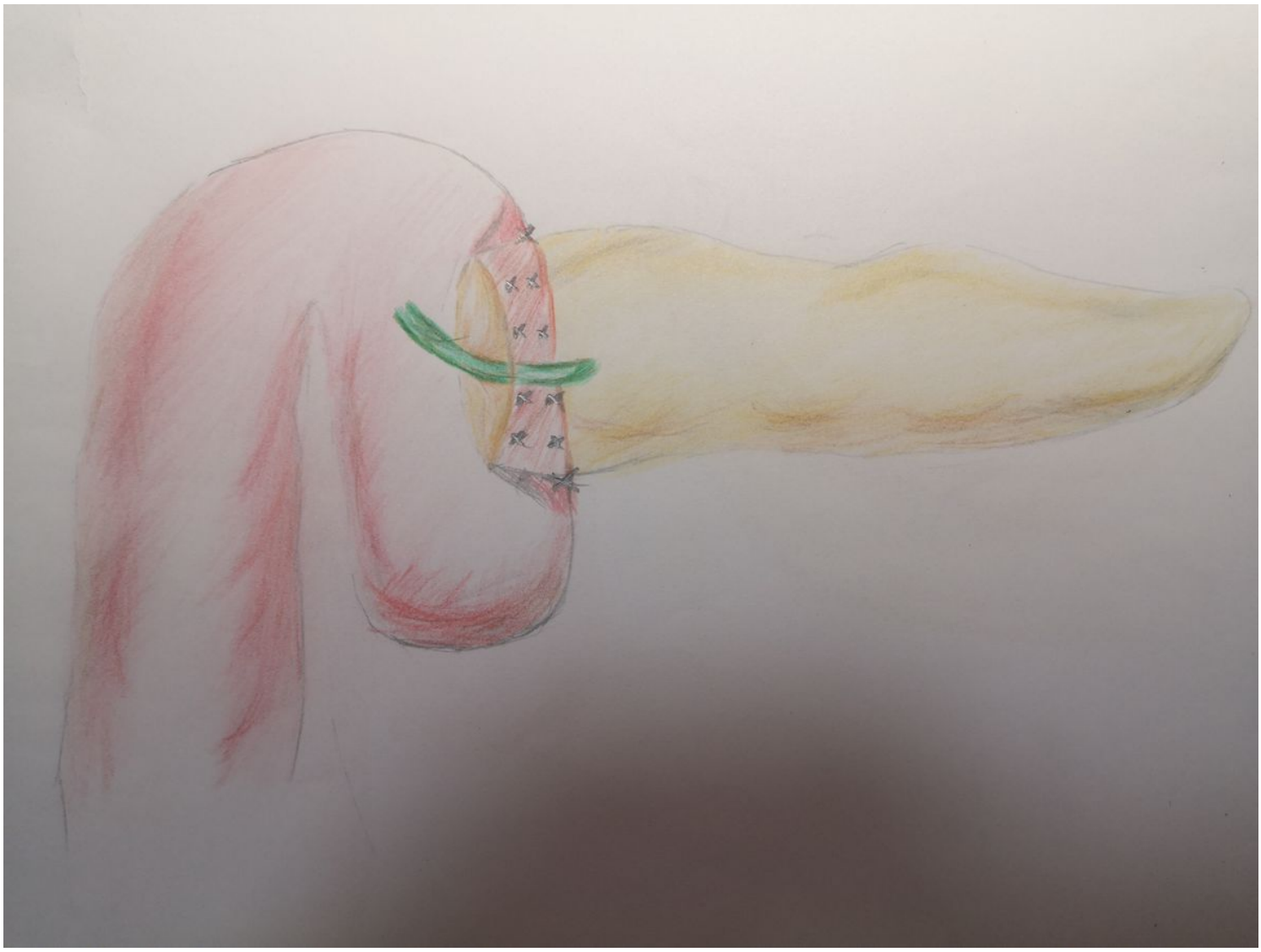

Figure 3