



ORIGINAL ARTICLE

Randomized controlled study of the effect of octreotide on pancreatic exocrine secretion and pancreatic fistula after pancreatoduodenectomy



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KEYWORDS

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Summary *Background:* Octreotide is known to decrease the rate of postoperative complication after pancreatic resection by diminishing exocrine function of the pancreas. The aim of this study was to evaluate the effect of octreotide in decreasing exocrine excretion of pancreas and preventing pancreatic fistula.

Materials and methods: Prospective randomized trial was conducted involving 59 patients undergoing pancreaticoduodenectomy for either malignant or benign tumor, 29 patients were randomized to receive octreotide; 30 patients allotted to placebo. All pancreaticojejunal anastomosis was performed with external stent of negative-pressured drainage and the amount of pancreatic juice through the external stent was measured until postoperative 7th day. Pancreatic fistula was recorded.

Results: There were no differences in demographics, pancreatic texture and pancreatic duct diameter between the octreotide and placebo group. The median output of pancreatic juice was not significantly different between both groups during 7 days after surgery. When the patients were stratified according to the diameter of pancreatic duct (duct ≤ 5 mm, > 5 mm), there were no significant differences in daily amount of pancreatic juice, however, when

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stratified according to pancreatic texture, median output of pancreatic juice was significantly lower in patients with hard pancreas compared with those with soft pancreas from 5 day to 7 day after surgery ($p < 0.05$). No significant differences in pancreatic fistula and postoperative complications were found between the octreotide and placebo groups.

Conclusions: Prophylactic octreotide is not effective to inhibit the exocrine secretion of the remnant pancreas and does not decrease the incidence of pancreatic fistula after pancreaticoduodenectomy.

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1. Introduction

Since pancreaticoduodenectomy (PD) is the gold standard in the treatment of periampullary tumor, the operative mortality of PD has declined, morbidity remains high, up to 50%.^{1,2} Postoperative pancreatic fistula (POPF) is the major cause of morbidity after PD with reported incidence ranging from 10 to 35%.^{2–4} Because POPF may lead to secondary septic and hemorrhage complication, organ failure and death, various attempts in pancreatic anastomosis have been made to decrease the incidence of POPF. Adhesive sealants around the anastomosis, use of transanastomotic stents and use of various systemic pharmacological agents are used to decrease the incidence of POPF.⁵

Somatostatin and its analogues had been presumed to reduce the rate of POPF by inhibitory effect on the exocrine secretion of the pancreas and facilitate closure of pancreatic leakage.^{6,7} During 1990s, several double-blinded multicenter randomized controlled trials (RCTs) have suggested a statistically significant decrease in overall postoperative complications after pancreatectomy with the use of perioperative octreotide.^{8–10} These studies had a limit of majority of patients with chronic pancreatitis who would be expected to show a lower incidence of pancreatic fistula. In 2000s, studies reported no statistically significant benefit of the perioperative use of octreotide.^{11–14} In meta-analyses series, the results are also conflicting about the effect of somatostatin and its analogues on postoperative complications.^{15–19}

Other studies have attempted to verify the effect of somatostatin on remnant exocrine secretion and related morbidity in patients undergoing PD.^{20,21}

Despite the conflicting results, octreotide is tend to be administered on surgeon's perception of risk factor of future POPF development such as soft pancreas, small pancreatic duct.

The aim of this study was to evaluate the effect of prophylactic octreotide in decreasing exocrine secretion of pancreas after PD and to compare the efficacy of this drug in preventing POPF and postoperative complications.

2. Methods

2.1. Inclusion criteria, randomization

Sample size was calculated based on the incidence of POPF for 10% of the patients with octreotide and for 40% without

octreotide treatment. On assumption of one sided confidence level 95% and a power of 80%, 29 patients were needed in each group. This study was registered at clinicaltrials.gov (NCT02920567).

After approval by the Institutional Review (XC12MI-MI0138V), patients undergoing elective PD for periampullary tumor between January 2014 and December 2017 in Department of Surgery at our Hospital were enrolled this trial on an intention to treat basis (Fig. 1). Patients whose surgery converted to a different surgical procedure such as bypass surgery, total pancreatectomy or segmental resection of bile duct cancer were excluded. Enrolled patients were randomized to either the octreotide or the placebo group. The randomization process was carried out by means of a randomly generated number pattern. Patients with the octreotide group received 100 μ g (1 ml) subcutaneously preoperatively and every 8 h after surgery for 7 days. Patients in the placebo group received same amount of saline administered in a similar manner.

2.2. Surgical technique

All patients received prophylactic antibiotics. In all patients PD was performed as a partial pancreatectomy with pylorus preservation or distal gastrectomy. Pancreatic anastomosis was retrocolic, Roux-en-Y 2-layered, end-to-side pancreaticojejunostomy with the use of fine monofilament absorbable sutures. The site of anastomosis was performed about 15 cm distant from jejunal stump. The outer layer between the pancreatic capsule and the jejunum was performed in continuous fashion with 5-0 monofilament nonabsorbable suture and the inner row of interrupted sutures included over 8 stitches posteriorly and anteriorly from pancreatic duct to jejunal mucosa with 5-0 monofilament absorbable sutures. A long external stent after making side hole was inserted and secured to one of duct-to mucosa stitch to prevent catheter migration. A small jejunotomy at jejunal stump was made to allow the catheter to be externalized through a stab incision in the left side abdominal wall. A purse string suture was used to reinforce the jejunotomy site through which external catheter exited. Two close suction drainage tubes (Jackson--Pratt silicone flat drain; Fortune Medical Instrument Corp., Taipei Hsien, Taiwan) were placed to anterior and the other posterior to the pancreaticojejunostomy anastomosis. The external end of pancreaticojejunostomy stent was

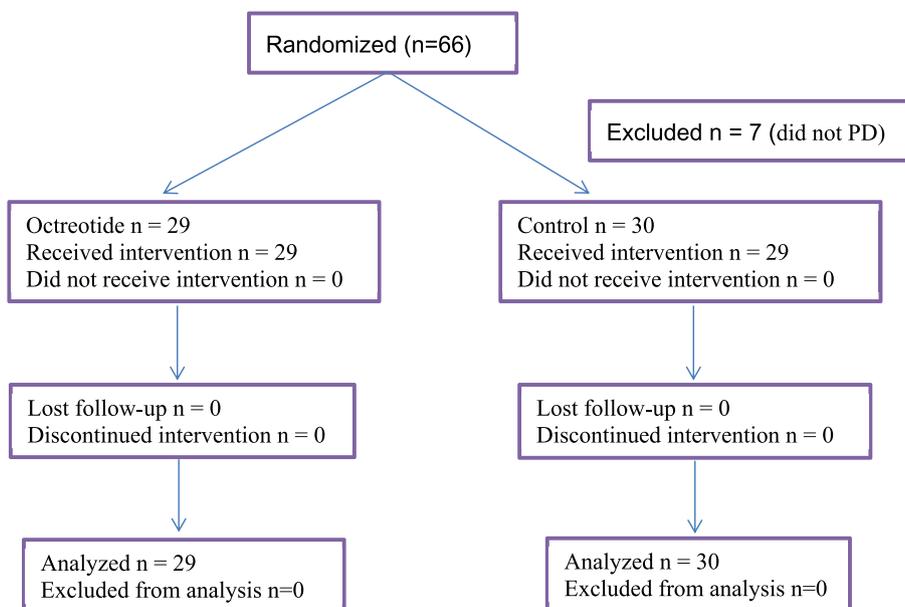


Figure 1 Selection of the study group according to CONSORT template.

connected to negative pressure (Jackson–Pratt) for effective drainage of pancreatic juice.

Pancreatic duct diameter was measured at the natural status after pancreatic transection. Pancreatic hardness was assessed subjectively based on visual and tactile sense.

2.3. Perioperative management and data collection

Nasogastric tubes were removed at 1 day after surgery. Sips of water was started at 4–5 days after surgery if there was no clinical evidence of leakage of any anastomosis and then, oral diet was advanced daily. Routine computed tomography was performed at 5–7 days after surgery.

Amylase in drainage fluid were measured on day 3,5,7 after the operation. POPF was graded as per International Study Group of Pancreatic Fistula as ISGPF grades A, B or C.²² Intraabdominal drainage tubes were started to be removed at day 7 one by one if there was no evidence of POPF. Daily pancreatic juice output through external stent with negative pressure was measured for 7 days during the postoperative period. Primary endpoint was pancreatic juice output. Secondary endpoints were the incidence of POPF and postoperative complications.

Perioperative demographic and clinical data about the details of the operation, including information on pancreatic texture, duct size, pathological diagnosis, postoperative complications were collected prospectively. Hospital stay was calculated from the day of surgery.

2.4. Statistical analyses

Patient demographic and clinical characteristics were compared between the octreotide and placebo group. Continuous data were described as median with range. The Mann–Whitney U-test or Student’s t test was used for statistical analysis of continuous data, and the Chi square test or Fisher’s exact test was employed to assess the

categorical data. The Variables with *P* value of <0.05 were considered to be statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp, Armonk, New York, US).

3. Results

3.1. Patients’ characteristics

A total of 66 consecutive patients were scheduled for PD and randomized to the study. Seven patients were excluded because conversion to a different operation (segmental resection of bile duct or transduodenal ampullectomy). Fifty-nine patients underwent elective PD and 29 patients received prophylactic octreotide and 30 patients’ saline doses. Both groups were comparable with respect to demographics (Table 1.) The median age was 71 (range: 45–85) in the octreotide group and 70 (range: 53–80) in the placebo group. There were no differences between groups in terms of gender, body mass index, operation time, estimated blood loss, transfusion. Most pancreaticoduodenal resections were performed with pylorus preservation. The most common disease was distal common bile duct cancer followed by pancreatic cancer, ampullary cancer and others.

3.2. Pancreatic characteristics and exocrine secretions

Pancreatic texture and duct diameter were summarized in Table 2. Most pancreas (76%) were soft and about 90% of pancreatic duct was less than 5 mm. Daily amount of pancreatic juice through the external stent with negative pressure increased steadily up to 7 days. No significant differences in median daily output were observed

Table 1 Patients characteristics of octreotide and placebo group.

	Octreotide (n = 29)	Placebo (n = 30)	P value
Age	71 (45–85)	70 (53–80)	0.12
Sex			
Male	14 (48)	18 (60)	0.44
Female	15 (52)	12 (40)	
Body mass index (kg/m ²)	23.6 (16.2–27.7)	22.6 (16.9–30.4)	0.44
CA 19-9 (UI/mL)	102.7 (3.7–2000)	38.6 (0–2000)	0.29
Operation time	330 (235–474)	323 (238–447)	0.28
Estimated blood loss	500 (200–4010)	500 (200–1500)	0.80
Transfusion			
Yes	5 (17)	3 (10)	0.47
No	24 (83)	27 (90)	
Diagnosis			
Bile duct cancer	13 (45)	11 (37)	0.70
Pancreatic cancer	9 (31)	8 (27)	
Ampullary cancer	5 (17)	6 (20)	
Others	2 (7)	5 (16)	

Continuous data were described as median with range and categorical data as number with percentage.

Table 2 Pancreatic texture and pancreatic duct diameter octreotide and placebo group.

	Octreotide (n = 29)	Placebo (n = 30)	P value
Pancreas texture			
Soft	22 (76)	23 (77)	1.0
Hard	7 (24)	7 (23)	
Diameter of pancreatic duct			
≤5 mm	26 (90)	26 (87)	1.0
>5 mm	3 (10)	4 (13)	

Data were described as number with percentage.

between the octreotide and placebo groups (Table 3). When the patients were stratified according to the diameter of pancreatic duct (duct ≤5 mm, > 5 mm), there was no significant difference in daily amount of pancreatic juice between both groups (Table 4). When the patients were stratified according to pancreatic texture, no significant differences in daily output from 1 day to 4 day after surgery emerged between the octreotide and placebo groups. However, from 5 day to 7 day after surgery,

Table 3 Amount of Pancreatic juice during postoperative days 1–7.

Postoperative day	Octreotide (n = 29)	Placebo (n = 30)	P value
1 day	7.5 (0–55)	5 (0–100)	0.51
2 day	32 (0–120)	27 (0–280)	0.93
3 day	52 (0–195)	70 (0–250)	0.98
4 day	77 (0–240)	76 (0–310)	0.66
5 day	107 (0–340)	54 (0–381)	0.31
6 day	124 (0–365)	44 (0–455)	0.22
7 day	115 (0–455)	75 (0–685)	0.44

Data were described as median with range.

patients with hard pancreas showed significantly less pancreatic juice ($p < 0.05$) compared with patient with soft pancreas (Table 4).

3.3. Postoperative courses

Postoperative courses of all patients were summarized in Table 5. Median postoperative day for soft diet was usually 7 days (4–11). There was no mortality except one patient who recovered to sips of water at 4 day after surgery, succumbed to sudden death because of being pulmonary thromboembolism. In octreotide group, relaparotomy was performed in 4 patients for bleeding control, wound repair, irrigation and drainage for abscess and pancreatic leakage; in placebo group, reoperation in 3 patients because of pancreatic leakages. Completion pancreatectomy was used for 4 patients with pancreatic leakage. One patient after completion pancreatectomy underwent another operation (for bile leakage) the other 3 patients recovered well. One patient in octreotide group needed angiographic intervention for control of pseudoaneurysmal rupture. The incidence of POPF was similar in both groups. The rate of clinically relevant POPF was 3% in the octreotide group and 17% in placebo group ($p = 0.20$). One patient with grade C POPF in placebo group have taken a long-term steroid because of Bechet's disease. The median postoperative length of hospital stay was 13 days (4–50) in the octreotide group and 13 days (9–85) in the placebo group.

4. Discussion

Somatostatin and its analogues decrease exocrine and endocrine pancreatic secretion by binding the somatostatin receptors on the exocrine and endocrine cells, and decrease the secretion of cells.²³ The role of somatostatin administered by i.v. infusion was investigated by some RCTs. In the RCTs by Guillat et al, the analysis failed to demonstrate a significant decrease in pancreatic juice

Table 4 Pancreatic juice out according to pancreatic texture and pancreatic duct diameter.

POD	Soft (n = 45)	Hard (n = 14)	P value	P-duct ≤ 5 mm (n = 52)	P-duct > 5 mm (n = 7)	P value
1 day	5 (0–85)	10 (0–100)	0.58	5 (0–100)	0 (0–15)	0.19
2 day	32 (0–280)	27 (5–95)	0.35	30 (0–280)	15 (10–70)	0.28
3 day	70 (0–250)	32 (0–110)	0.06	70 (0–250)	19 (0–172)	0.20
4 day	87 (0–310)	36 (4–185)	0.28	80 (0–310)	15 (0–210)	0.51
5 day	116 (0–381)	32 (2–240)	0.04	90 (0–380)	110 (0–381)	0.64
6 day	151 (0–455)	24 (0–240)	0.01	100 (0–455)	136 (0–365)	0.76
7 day	135 (0–685)	19 (0–289)	0.02	85 (0–685)	191 (1–455)	0.71

Data were described as median with range.

POD: postoperative day.

Table 5 Progress of patients and POPF.

	Octreotide (n = 29)	Placebo (n = 30)	P value
POD of gas out	3 (2–5)	3.5 (2–5)	0.13
POD for sips	5 (4–6)	5 (3–8)	0.45
POD for soft diet	7 (5–8)	7 (4–11)	0.79
POPF			
None	22 (76)	15 (50)	0.16
Grade A	6 (21)	10 (33)	
Grade B	0	2 (7)	
Grade C	1 (3)	3 (10)	
Complication			
Present	7 (24)	5 (16)	0.33
Absent	22 (76)	26 (84)	
Hospital stay	13 (4–50)	13 (9–85)	0.68

Continuous data were described as median with range and categorical data as number with percentage.

POD: postoperative day, POPF: postoperative pancreatic fistula.

output and enzyme production following somatostatin infusion. However, they reported that somatostatin reduced incidence of POPF from the pancreatic remnant.²⁰ In the RCT by Shan et al found that the amount of exocrine secretion during the period of infusion of somatostatin decreased to about half in the somatostatin group in comparison to the placebo group within the first 7 days with marginal significance ($p = 0.06$)²¹. Fernandez-Cruz et al in their RCT reported that morbidity did not differ significantly between the octreotide group and placebo group and failed to demonstrate an inhibitory effect of octreotide on exocrine pancreatic secretion.²⁴ Of previous studies of pancreatic exocrine secretion, the external end of the catheter for pancreatic juice drainage was connected by gravitational drainage.^{20,21,24} However, this study has drained pancreatic juice on negative pressure by applying closed suction (Jackson Pratt bag) to the external end of the catheter, which facilitates drainage effectively than gravitational drainage. To the authors' knowledge, this is the first study to apply negative pressure to pancreatic juice drainage.

The current study showed prophylactic octreotide to lack of effect in reducing the exocrine secretion of the pancreas by measuring the amount of negatively drained pancreatic juice through external stent. The amount of

pancreatic juice according to duct diameter was also not different, however, hard texture of pancreas was associated with a decrease in median daily pancreatic juice and especially, pancreatic exocrine secretion was significantly lower in patients with hard pancreas at 5–7 days after surgery. In patients with normal soft pancreas, pancreatic juice increased as oral diet started at 4–5 days after surgery, however, hard pancreas failed to respond with oral diet due to its damage from the disease. The present study found that pancreatic adenocarcinoma was most commonly associated with hard texture (10/17, 59%), followed by ampullary cancer (2/11, 18%) bile duct cancer (2/24, 8%). Mastumoto et al reported that patients with pancreatic adenocarcinoma showed an abnormal secretory function based on stool elastase.²⁵

Early studies of somatostatin analogues favored the use of octreotide and found a decreased in pancreatic complications,^{8–10,26} however, recent RCTs and meta-analysis of RCTs showed that the use of the drug did not significantly reduce incidences of pancreatic fistula, total pancreas-specific complications, delayed gastric emptying, mortality or hospital stay.^{12–19} As the ISGPF definition and grading of POPF has gained widespread acceptance, trials comparing the use of somatostatin or its analogue have reported POPF using the ISGPF definition and have demonstrated no difference in the incidence of POPF with or without use of the drugs.^{12,17,20} In this study, the overall rate of POPF was 24% in octreotide group and 50% in placebo group, and this result is comparable to the RCT of soft pancreas and non-dilated duct by Kurumboor et al (grade A POPF 44–49% in both groups).²⁷ When consideration of grade B or C, there was one (3%) of clinically relevant POPF in octreotide group and 5 (17%) in placebo group. A trend towards decrease in octreotide group was observed in clinically significant POPF, however, it did not reach statistical significance ($p = 0.20$), probably a study with a larger sample size would show up the clinical implication of this difference. There was no statistical difference with respect to grades A, B and C POPF in both groups as well. There was no difference in overall complications, and particularly there was no difference in the reoperation rate as well.

In conclusion, this randomized controlled trial suggested that the effect of prophylactic octreotide on pancreatic exocrine secretion was proven to be not effective. Furthermore, the use of this drug in patients undergoing PD does not decrease rate of POPF or overall morbidity.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

- Balcom JHT, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch Surg*. 2001;136:391–398.
- Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. *Ann Surg*. 2006;244:10–15.
- Gouma DJ, van Geenen RC, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. *Ann Surg*. 2000;232:786–795.
- Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. *Ann Surg*. 1997;226:248–257. discussion 257–260.
- Poon RT, Lo SH, Fong D, Fan ST, Wong J. Prevention of pancreatic anastomotic leakage after pancreaticoduodenectomy. *Am J Surg*. 2002;183:42–52.
- Pederzoli P, Bassi C, Falconi M, Albrigo R, Vantini I, Micciolo R. Conservative treatment of external pancreatic fistulas with parenteral nutrition alone or in combination with continuous intravenous infusion of somatostatin, glucagon or calcitonin. *Surg Gynecol Obstet*. 1986;163:428–432.
- Prinz RA, Pickleman J, Hoffman JP. Treatment of pancreatic cutaneous fistulas with a somatostatin analog. *Am J Surg*. 1988;155:36–42.
- Buchler M, Friess H, Klempa I, et al. Role of octreotide in the prevention of postoperative complications following pancreatic resection. *Am J Surg*. 1992;163:125–130. discussion 130–121.
- Montorsi M, Zago M, Mosca F, et al. Efficacy of octreotide in the prevention of pancreatic fistula after elective pancreatic resections: a prospective, controlled, randomized clinical trial. *Surgery*. 1995;117:26–31.
- Pederzoli P, Bassi C, Falconi M, Camboni MG. Efficacy of octreotide in the prevention of complications of elective pancreatic surgery. Italian Study Group. *Br J Surg*. 1994;81:265–269.
- Barnett SP, Hodul PJ, Creech S, Pickleman J, Arahna GV. Octreotide does not prevent postoperative pancreatic fistula or mortality following Pancreaticoduodenectomy. *Am Surg*. 2004;70:222–226. discussion 227.
- Hesse UJ, DeDecker C, Houtmeyers P, et al. Prospectively randomized trial using perioperative low-dose octreotide to prevent organ-related and general complications after pancreatic surgery and pancreatico-jejunostomy. *World J Surg*. 2005;29:1325–1328.
- Suc B, Msika S, Piccinini M, et al. Octreotide in the prevention of intra-abdominal complications following elective pancreatic resection: a prospective, multicenter randomized controlled trial. *Arch Surg*. 2004;139:288–294. discussion 295.
- Yeo CJ, Cameron JL, Lillemoe KD, et al. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. *Ann Surg*. 2000;232:419–429.
- Connor S, Alexakis N, Garden OJ, Leandros E, Bramis J, Wigmore SJ. Meta-analysis of the value of somatostatin and its analogues in reducing complications associated with pancreatic surgery. *Br J Surg*. 2005;92:1059–1067.
- Gurusamy KS, Koti R, Fusai G, Davidson BR. Somatostatin analogues for pancreatic surgery. *Cochrane Database Syst Rev*. 2010:CD008370.
- Koti RS, Gurusamy KS, Fusai G, Davidson BR. Meta-analysis of randomized controlled trials on the effectiveness of somatostatin analogues for pancreatic surgery: a Cochrane review. *HPB (Oxford)*. 2010;12:155–165.
- Li-Ling J, Irving M. Somatostatin and octreotide in the prevention of postoperative pancreatic complications and the treatment of enterocutaneous pancreatic fistulas: a systematic review of randomized controlled trials. *Br J Surg*. 2001;88:190–199.
- Zeng Q, Zhang Q, Han S, et al. Efficacy of somatostatin and its analogues in prevention of postoperative complications after pancreaticoduodenectomy: a meta-analysis of randomized controlled trials. *Pancreas*. 2008;36:18–25.
- Gouillat C, Chipponi J, Baulieux J, Partensky C, Saric J, Gayet B. Randomized controlled multicentre trial of somatostatin infusion after pancreaticoduodenectomy. *Br J Surg*. 2001;88:1456–1462.
- Shan YS, Sy ED, Lin PW. Role of somatostatin in the prevention of pancreatic stump-related morbidity following elective pancreaticoduodenectomy in high-risk patients and elimination of surgeon-related factors: prospective, randomized, controlled trial. *World J Surg*. 2003;27:709–714.
- Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery*. 2005;138:8–13.
- Lembcke B, Creutzfeldt W, Schleser S, Ebert R, Shaw C, Koop I. Effect of the somatostatin analogue sandostatin (SMS 201-995) on gastrointestinal, pancreatic and biliary function and hormone release in normal men. *Digestion*. 1987;36:108–124.
- Fernandez-Cruz L, Jimenez Chavarria E, Taura P, Closa D, Boado MA, Ferrer J. Prospective randomized trial of the effect of octreotide on pancreatic juice output after pancreaticoduodenectomy in relation to histological diagnosis, duct size and leakage. *HPB (Oxford)*. 2013;15:392–399.
- Matsumoto J, Traverso LW. Exocrine function following the whipple operation as assessed by stool elastase. *J Gastrointest Surg*. 2006;10:1225–1229.
- Friess H, Beger HG, Sulkowski U, et al. Randomized controlled multicentre study of the prevention of complications by octreotide in patients undergoing surgery for chronic pancreatitis. *Br J Surg*. 1995;82:1270–1273.
- Kurumboor P, Palaniswami KN, Pramil K, et al. Octreotide does not prevent pancreatic fistula following pancreatoduodenectomy in patients with soft pancreas and non-dilated duct: a prospective randomized controlled trial. *J Gastrointest Surg*. 2015;19:2038–2044.