

## Review Article

## Diagnosis and treatment of pancreas divisum: A literature review

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## ABSTRACT

**Background:** Pancreas divisum is a congenital embryological disease caused by a lack of fusion between the ventral and dorsal pancreatic ducts in the early stages of embryogenesis. Recurrent acute pancreatitis, chronic pancreatitis or chronic abdominal pain are the main clinical syndromes at presentation and occur in only 5% of the patients with pancreas divisum. This review aimed to discuss diagnosis and treatment strategies in patients with symptomatic pancreas divisum.

**Data sources:** We report a literature review from 1990 up to January 2018 to explore the various diagnostic modalities and surgical techniques and results reported in the surgical treatment of pancreas divisum.

**Results:** There are limited reports available on this topic in the literature. We analyzed and described the main indications in the treatment of pancreas divisum, focusing on surgical treatment and a discussion of the different approaches. Furthermore, we report the results from our experience in two cases of pancreas divisum treated by pancreatic head resection with segmental duodenectomy (the Nakao procedure).

**Conclusions:** Pancreas divisum is a common pancreatic malformation in which only a few patients develop a symptomatic disease. Surgical treatment is needed in case of endoscopic drainage failure and in cases complicated with chronic pancreatitis and local complications. Many techniques, of greater or lesser complexity, have been proposed.

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## Introduction

Pancreas divisum is characterized by the persistence of two drainage systems: the main duct (Wirsung duct) that originates from the ventral pancreas and drains the pancreatic head through the major papilla, and the Santorini duct (originating from the dorsal pancreas) that drains the body and the tail through the minor papilla [1,2]. In pancreas divisum, the Santorini duct represents the main drainage channel in contrast to the Wirsung duct, which takes on a marginal role.

Pancreas divisum represent the main pancreatic anatomical variation with an incidence of 4.5%, as reported in a recent review [3], with 5% of patients with pancreas divisum developing a symptomatic disease; these patients present recurrent acute pancreatitis (rAP), chronic pancreatitis (CP) and chronic abdominal pain (CAP). The pathogenesis of the symptomatic case is also discussed. In pancreas divisum, pancreatic drainage occurs mainly through the minor papilla, and the small size of the minor papilla leads to high intrapancreatic duct pressure. Pancreas divisum is

classified into three types: type 1 (the most common), the ventral and dorsal pancreatic ducts are completely divided; type 2, the ventral pancreatic duct is absent; and type 3, a thin duct between the two systems is present [4].

Recent studies suggest that pancreas divisum may be a co-factor in the development of pancreatitis for other reasons. Bertin et al. [5] observed that the frequency of pancreas divisum is the same in patients with idiopathic pancreatitis when compared with control subjects, demonstrating that pancreas divisum alone is not a cause of pancreatitis, and postulated that pancreas divisum may act as a co-factor in patients with genetic pancreatitis, especially in those with *CFTR* mutations.

## Diagnosis and treatment

Endoscopic retrograde cholangiopancreatography (ERCP) is considered as the gold standard procedure for the diagnosis of pancreas divisum [6,7], although ERCP is an invasive test requiring sedation and leads to a 10%–15% complication rate with an additional rate of up to 10% post-ERCP pancreatitis. Pancreas divisum can be diagnosed by cannulation of the minor papilla for the

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visualization of the dorsal pancreatic duct in 90%–95% of patients, especially when needle-tip endoscopic catheters are used [8,9].

Magnetic resonance cholangiopancreatography (MRCP) has emerged as a non-invasive imaging modality for the diagnosis of pancreas divisum. Secretin enhancement can improve visualization of the pancreas; therefore, secretin-enhanced MRCP (S-MRCP) has been suggested to enhance the detection of congenital pancreaticobiliary malformations, including pancreas divisum. The pooled sensitivity and specificity for the diagnosis of pancreas divisum were reported to be 52% and 97% for MRCP, and 85% and 97% for S-MRCP, respectively [10].

In our opinion, MRCP and S-MRCP can be considered as the first option modality in the diagnosis of pancreas divisum, and ERCP has to be reserved for uncertain cases and in the treatment of symptomatic cases.

### Endoscopic treatment

Up to now, ERCP including papillotomy of minor papilla, with or without plastic stent implantation, is the first choice for therapeutic intervention in patients with symptomatic pancreas divisum. Good response rates and a low level of complications make it the first line of treatment for these patients.

In a systematic review included studies from 1950 to 2008, overall reported response rates after ERCP for rAP, CP and CAP were 81.2%, 68.8% and 53.1%, respectively [11]. The most recent systematic review in 2014 gave a response rate of 76%, 42% and 33% for rAP, CP, and CAP, respectively [9]. In 2016, Lu et al. [12] described a larger retrospective study with 141 procedures for pancreas divisum. Endoscopic pancreatic sphincterotomy (44.68%), bougienage (26.95%), pancreatic ductal stone extraction (19.15%), endoscopic nasopancreatic drainage (21.99%), and endoscopic retrograde pancreatic drainage (56.74%) were performed with an overall response rate of 62.32%. Post endoscopy pancreatitis (PEP), infection, and hemorrhage were 9.93%, 3.55%, and 0.71%, respectively [12]. Michailidis et al. [13] confirmed that endoscopic efficacy in pancreas divisum is 67.5%.

In case of failure of plastic stent placement, the use of removable fully covered, self-expandable metal stents have been recently described with a successful rate of 90% at 3 months [14].

### Surgery

Surgery has to be considered in case of the failure of the endoscopic treatment in symptomatic patients when a normal pancreas is present, or in case of CP and local complications, such as common bile duct stricture or main pancreatic duct stenosis. Surgical strategy aims to treat local complications and to optimize the pancreatic drainage. Different surgical treatments have been described: sphincteroplasty, duodenopancreatectomy and duodenum-preserving pancreatic head resection are the most performed treatments (Table 1).

Recently, Hafezi et al. published a meta-analysis of 1887 patients with pancreas divisum treated with surgery or endoscopically, and concluded that surgical treatment may be superior to endoscopy in terms of success rate, complication rate and re-intervention rate [15]. Symptom improvement was significantly obtained in surgically treated patients (72% for the surgical group vs. 62.3% for the endoscopic group). Moreover, the complication rate and re-intervention rate of endoscopic procedures are significantly higher than those of surgery (31.3% vs. 23.8%, and 28.3% vs. 14.4%, respectively). This study has an important limitation which is the study's heterogeneity, involving clinical, methodological and statistical biases. In our opinion, surgery must be considered in a very few selected patients, and only in the case of the failure of endoscopic treatment. Up to now the evidence is not sufficient and

**Table 1**  
Surgical procedures in the treatment of pancreas divisum.

Procedures	Description
Decompression procedure	
Sphincteroplasty	• Transduodenal surgical sphincterotomy/sphincteroplasty
Pustrow procedure	• Dissection of the pancreatic duct throughout the body and tail of the gland • Longitudinal side-to-side pancreaticojejunostomy
Demolitive procedure	
PPPD	• Pancreatoduodenectomy with pylorus preservation
Berge procedure	• Dissection of pancreatic head from portal vein and complete transection of neck • Subtotal excision of pancreatic head • Reconstruction with a Wirsung-jejunal anastomosis and a pancreaticojejunostomy anastomosis with Roux-en-Y jejunal loop
Frey procedure	• Longitudinal drainage of pancreatic duct • Local resection of pancreatic head
Bern modified procedure	• Local resection of pancreatic head • Single anastomosis (pancreaticojejunostomy) with Roux-en-Y jejunal loop
Nakao procedure	• Complete pancreatic head resection with segmental duodenectomy • Pancreatogastrostomy, end-to-end duodenoduodenostomy

PPPD: pylorus-preserving pancreatoduodenectomy.

further studies are needed to define precise selection criteria for surgical treatment.

In this paper we described the main surgical procedure and discussed surgical techniques and indications. In addition, we provided a literature review from 1990 up to January 2018; we searched the PubMed database for MEDLINE subheadings and key words “pancreas divisum” or “duodenum-preserving pancreatic head resection” or “pancreatic sphincteroplasty”. Only English articles and papers with more than five cases were selected for review.

#### Decompression procedure

##### Sphincteroplasty

During a sphincteroplasty procedure, a longitudinal duodenotomy is performed and the papilla identified. The papillary and choledochal sphincter are then divided. Identification of the Wirsung duct and section of common septum between the bile and pancreatic duct is realized, and the sphincteroplasty is completed by suturing the biliopancreatic sept to the mucosa.

Sphincteroplasty is the main surgical treatment for pancreas divisum before the endoscopic drainage era [8,16–23] (Table 2). Present indications are limited: in the last 10 years only a few series have been reported, such as Schneider et al. [16] who described a series of all 11 sphincteroplasty in patients with pancreas divisum and performs it in cases of soft pancreas with no signs of inflammatory or fibrotic changes in the pancreatic parenchyma. In three of these cases, a second operation was indicated for persisting symptoms of pancreatitis. Madura et al. [17] also described a series of 74 patients with pancreas divisum treated with surgical sphincteroplasty with a success rate of 63%. Sphincteroplasty is a highly complex technique and, despite its parenchyma sparing procedure, it is characterized by a low success rate. In our opinion, it should not be used as the first option in the surgical treatment of pancreas divisum.

##### Pustrow procedure

In case of advanced disease, where CP changes cause a ductal obstruction and a dilated main pancreatic duct, longitudinal side-to-side pancreaticojejunostomy can be performed.

**Table 2**  
Literature review of pancreas divisum treated with decompression procedures.

Studies	n	F/M	Median age (yr)	Sphincteroplasty				LPY			
				n	Clavien III-IV	Success rate	Reintervention rate	n	Clavien III-IV	Success rate	Reintervention rate
Bradley III et al. [8]	37	–	–	37	–	83.7%	–	–	–	–	–
Schneider et al. [16]	28	11/17	–	11	0	72%	–	–	–	–	–
Madura et al. [17]	74	–	–	74	–	63%	–	–	–	–	–
Schnelldorfer et al. [18]	21	10/11	40	–	–	–	–	21	–	90%	–
Varshney et al. [19]	5	4/1	34	2 + distal pancreatotomy	0	100%	–	1	0	100%	–
Tzovaras et al. [20]	6	4/2	–	6	0	50%	–	–	–	–	–
Siegel et al. [21]	25	–	35	–	–	–	–	–	–	–	–
Brenner et al. [22]	13	9/4	37	13	–	77%	–	–	–	–	–
Warshaw et al. [23]	88	–	–	88	–	70%	–	–	–	–	–

LPY: lateral pancreaticojejunostomy.

**Table 3**  
Literature review of pancreas divisum treated with demolitive procedures.

Studies	n	F/M	Median age (yr)	DPPHR				PPPD			
				n	Clavien III-IV	Success rate (%)	Reintervention rate	n	Clavien III-IV	Success rate	Reintervention rate
Schneider et al. [16]	28	11/17	–	10	20%	80%	–	4	1	96%	–
Varshney et al. [19]	5	4/1	34	1 Beger	0	100%	–	–	–	–	–
Vicente et al. [24]	2	0/2	54.5	2 Nakao	0	100%	–	–	–	–	–
Pappas et al. [25]	6	5/1	47	6 Frey	33%	87%	–	–	–	–	–
Schlosser et al. [26]	36	15/21	37.2	36 Beger	3.6%	81%	–	–	–	–	–

DPPHR: duodenum-preserving pancreatic head resection; PD: pancreatoduodenectomy; PPPD: pylorus-preserving pancreatoduodenectomy.

Schnelldorfer et al. [18] reported 21 cases of pancreas divisum with CP that submitted to the Pustrow procedure with a success rate of 90% (Table 2) [18].

#### Demolitive procedure

Relevant articles in the literature comparing the demolitive procedure in the treatment of pancreas divisum are insufficient. From amongst all surgical procedures, pancreatoduodenectomy—with or without pylorus preservation and duodenum-preserving pancreatic head resection—are the most known and applied (Table 3). The success rate varies from 80%–100% and a complication rate of 0–33% has been reported [16,19,24–26]. The number of patients in these studies is small and the best technique has not yet been identified.

#### Pancreatoduodenectomy (PD) and pylorus-preserving pancreatoduodenectomy (PPPD)

PD with or without pylorus preservation represents the procedure of choice in these patients. The extent of resection in PD includes pancreatic head with duodenum and partial gastric resection. PPPD is a less aggressive procedure in which the stomach is preserved. When PD and PPPD are performed in high volume pancreatic centers, an operative mortality of 2%–5% is reported, with a success rate in the treatment of pancreas divisum of approximately 80% [27].

#### Duodenum-preserving pancreatic head resection (DPPHR)

Considering that PD has a high rate of complication and a not negligible rate of mortality in the treatment of a benign disease, DPPHR techniques have been reported, with the goal of minimizing the impact of surgery, and to preserve the enteroinsular axis in glucose homeostasis (Fig. 1)

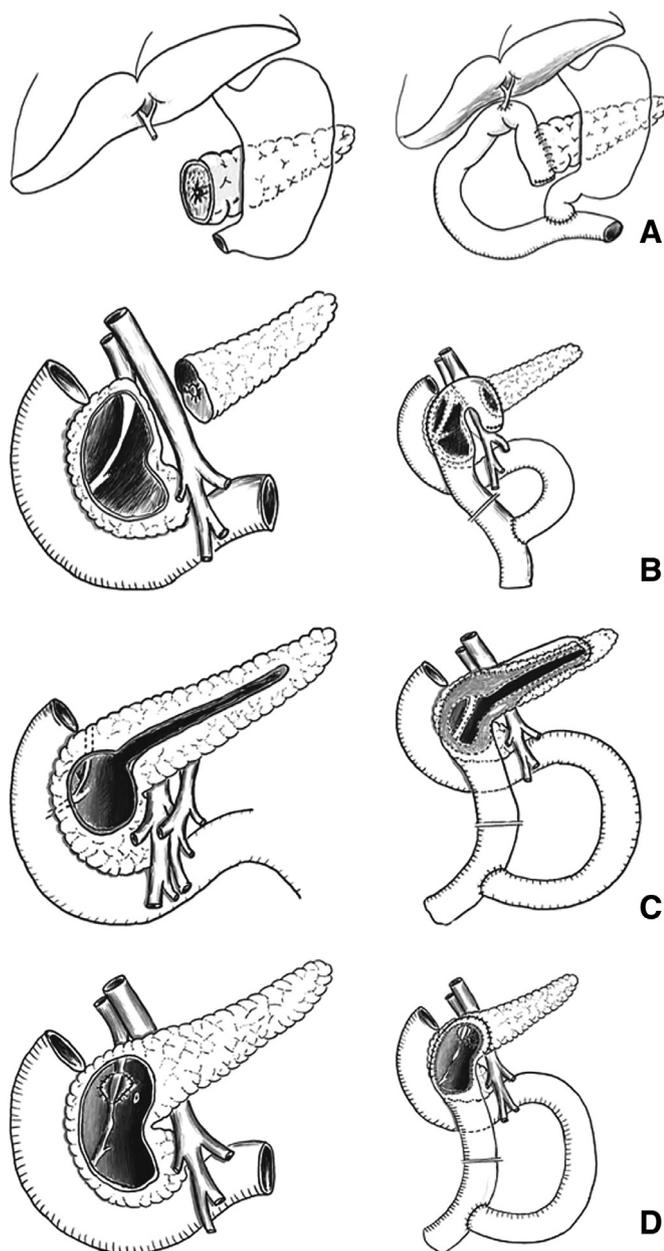
According to Beger et al. [28] introduced DPPHR procedure, the pancreas is divided at the level of the portal vein. The pancre-

atic head is then detached although not completely removed, thus preserving the duodenum and the deeper layer of pancreatic tissue. Reconstruction is then carried out with two anastomoses: the Wirsung-jejunal anastomosis and the pancreatic head-jejunal anastomosis so as to drain the pancreatic remnant and to cover the defect in the pancreatic head. If necessary, even the common bile duct can be drained in order to avoid ischemic complication or by-pass obstruction.

Frey et al. [29] presented a modified DPPHR resection which represents a hybrid technique between the Beger and Pustrow procedures. In the Frey technique the pancreatic head resection is smaller, and a laterolateral pancreaticojejunostomy is performed to drain the entire pancreatic duct. In this way, only a single anastomosis can be realized. This technique is not eligible in the case of pancreas divisum with chronic pancreatitis with a large inflammatory mass in the pancreatic head. However, it appears advantageous in cases with minor inflammatory component and can be suitable in solving obstruction in the left-sided pancreatic duct.

In the Bern modification procedure of the DPPHR [30], the excavation of the pancreatic head can be performed in an identical manner as the Berger procedure, however it differs from the Berger procedure as the pancreas is not divided at the level of the portal vein. Reconstruction can be performed by one single anastomosis between the pancreatic excavated head and a jejunal loop. This technique is suitable in cases in which an inflammatory mass is not associated with a stenosis of the left-sided duct. If required, a biliary jejunal anastomosis can be performed.

Nakao et al. described pancreatic head resection with segmental duodenectomy (PHRSD) in 1998 [31]. In this technique, a complete pancreatic head resection with segmental duodenectomy including the minor and major papilla is realized. The first portion of the duodenum is preserved maintaining the gastroduodenal artery and the anterior superior pancreaticoduodenal artery. The third

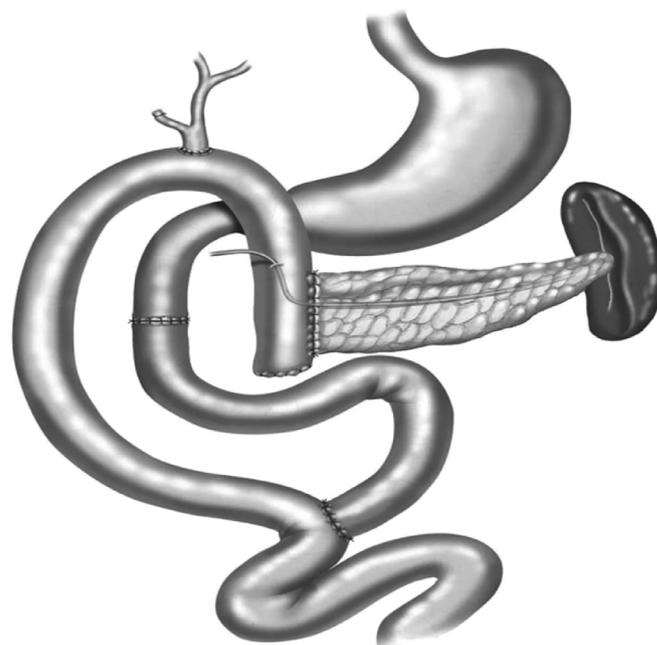


**Fig. 1.** Duodenum-preserving pancreatic head resection (DPPHR) techniques. **A:** Pancreatoduodenectomy; **B:** Berger procedure; **C:** Frey procedure; **D:** Bern procedure.

and fourth portion of the duodenum are preserved conserving the anterior inferior pancreaticoduodenal artery. An end-to-end duododuodenostomy is performed and the biliary and pancreatic drainage are re-established with a pancreaticojejunostomy and hepaticojejunostomy in a Roux-en-Y anastomosis (Fig. 2).

Nakao et al. have reported 67 cases of pancreatic head resection with segmental duodenectomy [32,33]. This technique was proposed by Nakao for the treatment of intraductal papillary mucinous neoplasm (IPMN). In this population, mortality was null, pancreatic fistula occurred in 10% and 13% with types (alimentary tract reconstruction) A and B, respectively.

In our opinion, this technique should be considered in the case of pancreas divisum because it allows an anatomic complete head resection and avoids ischemic complication of the biliard duct and duodenum. In previous report [24], we described 2 cases of pancreas divisum treated with Nakao technique. Operative time



**Fig. 2.** Nakao procedure.

was 200 min and 240 min, and the post-operative stay was 11 and 14 days, respectively. In the second case, a pancreatic fistula was treated conservatively.

### Conclusion

Pancreas divisum is a benign congenital disease. In 5% of patients it can cause rAP, CP and CAP. Endoscopy is considered the first line treatment, and offers good results with acceptable complication rate. In our opinion, surgery remains the best option for symptomatic patients in cases of endoscopic failure.

Surgery offers a good success rate and several techniques have been described with acceptable complication rate; as reported in our experience Nakao technique should be considered as a surgical option in the treatment of pancreas divisum.

### Contributors

VE and QY proposed the study. FV and CR performed the research and wrote the first draft. IB, DH, DE, and FI collected and analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts. FV is the guarantor.

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### Ethical approval

This study was approved by the Ethics Committee of the Sanchinarro Hospital, San Pablo University.

### Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

## References

- [1] Kozu T, Suda K, Toki F. Pancreatic development and anatomical variation. *Gastrointest Endosc Clin N Am* 1995;5:1–30.
- [2] Wang DB, Yu J, Fulcher AS, Turner MA. Pancreatitis in patients with pancreas divisum: imaging features at MRI and MRCP. *World J Gastroenterol* 2013;19:4907–4916.
- [3] Dimitriou I, Katsourakis A, Nikolaidou E, Noussios G. The main anatomical variations of the pancreatic duct system: review of the literature and its importance in surgical practice. *J Clin Med Res* 2018;10:370–375.
- [4] Warshaw AL, Simeone JF, Schapiro RH, Flavin-Warshaw B. Evaluation and treatment of the dominant dorsal duct syndrome (pancreas divisum redefined). *Am J Surg* 1990;159:59–66.
- [5] Bertin C, Pelletier AL, Vullierme MP, Bienvenu T, Rebours V, Hentic O, et al. Pancreas divisum is not a cause of pancreatitis by itself but acts as a partner of genetic mutations. *Am J Gastroenterol* 2012;107:311–317.
- [6] Quest L, Lombard M. Pancreas divisum: opinio divisa. *Gut* 2000;47:317–319.
- [7] Kim HJ, Kim MH, Lee SK, Seo DW, Kim YT, Lee DK, et al. Normal structure, variations, and anomalies of the pancreaticobiliary ducts of Koreans: a nationwide cooperative prospective study. *Gastrointest Endosc* 2002;55:889–896.
- [8] Bradley EL 3rd, Stephan RN. Accessory duct sphincteroplasty is preferred for long-term prevention of recurrent acute pancreatitis in patients with pancreas divisum. *J Am Coll Surg* 1996;183:65–70.
- [9] Kanth R, Samji NS, Inaganti A, Komanapalli SD, Rivera R, Antillon MR, et al. Endotherapy in symptomatic pancreas divisum: a systematic review. *Pancreatology* 2014;14:244–250.
- [10] Rustagi T, Njei B. Magnetic resonance cholangiopancreatography in the diagnosis of pancreas divisum: a systematic review and meta-analysis. *Pancreas* 2014;43:823–828.
- [11] Liao Z, Gao R, Wang W, Ye Z, Lai XW, Wang XT, et al. A systematic review on endoscopic detection rate, endotherapy, and surgery for pancreas divisum. *Endoscopy* 2009;41:439–444.
- [12] Lu Y, Xu B, Chen L, Bie LK, Gong B. Endoscopic intervention through endoscopic retrograde cholangiopancreatography in the management of symptomatic pancreas divisum: a long-term follow-up study. *Gut Liver* 2016;10:476–482.
- [13] Michailidis L, Aslam B, Grigorian A, Mardini H. The efficacy of endoscopic therapy for pancreas divisum: a meta-analysis. *Ann Gastroenterol* 2017;30:550–558.
- [14] Tringali A, Vadalà di Prampero SF, Landi R, Bove V, Familiari P, Hamanaka J, et al. Fully covered self-expandable metal stents to dilate persistent pancreatic strictures in chronic pancreatitis: long-term follow-up from a prospective study. *Gastrointest Endosc* 2018;88:939–946.
- [15] Hafezi M, Mayschak B, Probst P, Büchler MW, Hackert T, Mehrabi A. A systematic review and quantitative analysis of different therapies for pancreas divisum. *Am J Surg* 2017;214:525–537.
- [16] Schneider L, Müller E, Hinz U, Grenacher L, Büchler MW, Werner J. Pancreas divisum: a differentiated surgical approach in symptomatic patients. *World J Surg* 2011;35:1360–1366.
- [17] Madura JA, Madura JA 2nd, Sherman S, Lehman GA. Surgical sphincteroplasty in 446 patients. *Arch Surg* 2005;140:504–513.
- [18] Schnelldorfer T, Adams DB. Outcome after lateral pancreaticojejunostomy in patients with chronic pancreatitis associated with pancreas divisum. *Am Surg* 2003;69:1041–1046.
- [19] Varshney S, Johnson CD. Surgery for pancreas divisum. *Ann R Coll Surg Engl* 2002;84:166–169.
- [20] Tzovaras G, Rowlands BJ. Santoriniplasty in the management of symptomatic pancreas divisum. *Eur J Surg* 2000;166:400–404.
- [21] Siegel JH, Cooperman AM, Pullano W, Hammerman H. Pancreas divisum: observation, endoscopic drainage, and surgical treatment results in 65 patients. *Surg Laparosc Endosc* 1993;3:281–285.
- [22] Brenner P, Duncombe V, Ham JM. Pancreatitis and pancreas divisum: aetiological and surgical considerations. *Aust N Z J Surg* 1990;60:899–903.
- [23] Warshaw AL, Richter JM, Schapiro RH. The cause and treatment of pancreatitis associated with pancreas divisum. *Ann Surg* 1983;198:443–452.
- [24] Vicente E, Quijano Y, Ferri V, Ielpo B, Diaz E, Caruso R, et al. Pancreas divisum: duodenal-preserving resection of the head of the pancreas and pancreatic head. Resection with second-portion duodenectomy. *Cir Esp* 2014;92:1032.
- [25] Pappas SG, Pilgrim CH, Keim R, Harris R, Wilson S, Turaga K, et al. The Frey procedure for chronic pancreatitis secondary to pancreas divisum. *JAMA Surg* 2013;148:1057–1062.
- [26] Schlosser W, Rau BM, Poch B, Beger HG. Surgical treatment of pancreas divisum causing chronic pancreatitis: the outcome benefits of duodenum-preserving pancreatic head resection. *J Gastrointest Surg* 2005;9:710–715.
- [27] Andersen DK, Frey CF. The evolution of the surgical treatment of chronic pancreatitis. *Ann Surg* 2010;251:18–32.
- [28] Beger HG, Siech M, Poch B. Duodenum-preserving total pancreatic head resection: an organ-sparing operation technique for cystic neoplasms and non-invasive malignant tumors. *Chirurg* 2013;84:412–420.
- [29] Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987;2:701–707.
- [30] Gloor B, Friess H, Uhl W, Büchler MW. A modified technique of the Beger and Frey procedure in patients with chronic pancreatitis. *Dig Surg* 2001;18:21–25.
- [31] Nakao A. Pancreatic head resection with segmental duodenectomy and preservation of the gastroduodenal artery. *Hepatogastroenterology* 1998;45:533–535.
- [32] Nakao A, Fernández-Cruz L. Pancreatic head resection with segmental duodenectomy: safety and long-term results. *Ann Surg* 2007;246:923–931.
- [33] Nakao A, Takeda S, Nomoto S, Kanazumi N, Kasuya H, Sugimoto H, et al. Pancreatic head resection with segmental duodenectomy for pancreatic neoplasms. *J Hepatobiliary Pancreat Sci* 2010;17:788–791.