Central pancreatectomy revisited

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ABSTRACT

Central pancreatectomy (CP) is a parenchyma-sparing alternative resection to distal pancreatectomy, for benign and low malignant potential tumors located on the pancreatic isthmus and/ or body. Pancreatic metastases of other neoplasia might also benefit after a CP, in selected patients. Dagradi and Serio described the modern technique of CP, while Iacono introduced it in current clinical practice. An open CP represents the standard, but there is an emerging role for the minimally-invasive approach, which might become a standard for CP in experienced centers, particularly for the robotic approach. The rationale of a CP was to preserve the postoperative pancreatic functions because it implies the loss of a minimal amount of normal pancreatic tissue. However, the real clinical benefit of a CP is still controversial. High overall morbidity and pancreatic fistula rates were reported after a CP. However, most of the complications after a CP have been conservatively managed, with almost zero mortality. A CP has a minimal impact on the postoperative pancreatic functions; the diabetes mellitus rate after a CP is significantly lower, compared with the distal pancreatectomies. A proper selection of candidates for a CP is recommended. Thus, tumors located on the pancreatic isthmus are more likely to benefit after a CP, because the alternative surgical technique in these patients is an extended left pancreatectomy, a procedure with increased risk of postoperative pancreatic insufficiencies. Individual patient-related factors should be taken into consideration in the selection of the patients. Thus, a CP should be used in young patients, non-obese and without diabetes mellitus, with a good biological status, which might be able to overcome the potential postoperative complications. A CP can be safely incorporated into an experienced pancreatic surgeon armamentarium, albeit it represents an uncommon pancreatic resection.

Abbreviations: Central pancreatectomy (CP); Physiologic and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM).

Key words: Central pancreatectomy; Parenchyma-sparing pancreatic resection; Benign/ low malignant pancreatic tumors; Pancreatic metastasis; Morbidity; Pancreatic fistula; Diabetes mellitus

INTRODUCTION

Central pancreatectomy (CP) takes part from the group of parenchyma-sparing pancreatic resections, and it was introduced in clinical practice as alternative to standard pancreatic resections (i.e., pancreaticoduodenectomy

and distal pancreatectomy), for a particular pathology. (1) The primary goal of a CP was to better preserve the postoperative pancreatic functions. (1) Currently, CP is considered a real alternative only to distal pancreatectomies. (2,3)

Benign and low malignant potential pancreatic lesions located on the pancreatic isthmus and/ or body represents the main indications for a CP (2,3), whenever a reasonable part of the distal pancreas can be preserved (i.e., ≥ 5 cm), in the absence of a distal pancreas atrophy. (4)

The functional benefits have been shown in some studies (2,3), but the clinical value of a CP is still a matter of debate and controversies. (5) Thus, the proponents of a CP argue with the very good functional results (2,6-10), while the opponents of the method highlights the high morbidity rates, widely considered as higher, compared with the standard pancreatic resections. (11-14) Even in high-volume centers for pancreatic resections, favorable for a CP, the percentages for this surgical procedure were reported to be less than 5.5% of all pancreatic resections. (8,9,15-19)

Beside a "central pancreatectomy", with the same significance were used the following terms: "median/medial/middle/ intermediate pancreatectomy", "mesopancreatectomy" or "segmental pancreatectomy". (4,20,21)

The aim of the present paper was to provide an up-to-date review of the indications, technical issues, and early and late outcomes after CP, based on the relevant literature.

A short history of central pancreatic resections – the Dagradi-Serio-Iacono operation

Several authors have suggested that the first central pancreatic resections were communicated by Guillemin in 1957 and Letton in 1959. (11,20,22) Actually, neither Guillemin (23), nor Letton (24) performed a true pancreatic resection, and only the reconstruction part is similar to that reported on the modern technique of CP. (4,21) Thus, Guillemin performed only a complete transection of the pancreatic isthmus, in a patient with chronic pancreatitis, and both pancreatic remnants were sutured to an omega shape jejunal loop. (23) Interestingly, the transection of the pancreas in Guillemin's patient was an unexpected intraoperative complication, because the surgeon first intended to do a side-to-side wirsung-jejunostomy. (23)

Letton's patient presented with a complete post-traumatic transection of the pancreas, and the proximal pancreatic stump was sutured, while the distal pancre-

atic remnant was anastomosed to a jejunal Roux en Y loop. (24)

It appears that the first true central pancreatic resection was performed in 1909 by Finney from the Johns Hopkins Hospital (United States). (25) Finney's patient presented with a centrally located pancreatic cystadenoma; a central pancreatic resection was performed, but the two pancreatic stumps were sutured together. (25) Interestingly, in 2012, Di Benedetto and co-workers suggested a duct-to-duct anastomosis of the remnant pancreatic stumps after CP. (20)

The paternity of the modern technique of CP belongs to the group of surgeons from the University of Verona (Italy). (1) Thus, in 1982 Dagradi and Serio performed the first CP for an insulinoma, and the technique was, furthermore, introduced in current clinical practice by Iacono. (1,4,26)

Although the technique of a CP was described in 1910 (25), with the modern version in 1984 (1), this conservative pancreatic resection was rarely performed till recently. Thus, 10 years ago no more than 100 patients with a CP were reported worldwide. (8,27) However, the number of patients with a CP has significantly increased in the last 10 years, and 963 patients were reported in 2010. (2)

It appears that the first laparoscopic CP was performed in 2003 by Baca, while the first robotic CP was performed in 2004 by Giulianotti. (21)

An excellent, comprehensive and well-documented overview of the history of central pancreatic resections was recently released by Iacono and co-workers. (21)

In summary, although the procedure was described many years ago, CP still represents, nowadays, an uncommon pancreatic resection. Dagradi and Serio described the modern technique of CP, while Iacono introduced it in current clinical practice. Thus, the Dagradi-Serio-Iacono operation for a CP is entirely justified.

Indications and contraindications for a central pancreatectomy – beyond the benign and low malignant potential pathology

A recent meta-analysis has shown that a CP was indicated mainly for a benign or low malignant potential pathology of the pancreatic isthmus and/ or body. (2) The same findings were reported in large single center experiences with CP (*table 1*). (6,7,9,10,16, 17,19,28-30)

A widely accepted indication for a CP is represented by a serous cystadenoma. (2) However, the feasibility of a parenchyma-sparing resection in a patient diagnosed with a serous cystadenoma should not change the

Table 1 - Large series with central pancreatectomies (≥ 25 patients)

Institution, year of publication	Period	No of patients	Age, years	Main indications	Lesion diameter, mm	Morbidity	Pancreatic fistula	Re-laparotomy for complications	Mortality	Follow -up time, months	Diabetes mellitus	Pancreatic exocrine insufficiency
San Raffaele Hospital, Milan, Italy, 2003 (7)	1990 - 2000	32	51	Neuroendocrine tumors, serous/ mucinous cystadenoma	34	62%	50%	3%	0%	66	10%	6.2%
Heidelberg University, Heidelberg, Germany, 2006 (29)	2001 - 2005	40	53	Chronic pancreatitis, serous cystadenoma	-	42%	10%	5%	2.5%	29	3%	-
University of Verona, Verona, Italy & Massachusetts General Hospital, Boston, USA, 2007 (9)	1990 - 2005	100	54	Neuroendocrine tumors, serous cystadenoma	26	58%	44%	0%	0%	54	4%	5%
Indiana University, Indianapolis, USA, 2008 (17)	1998 - 2007	34	49	Chronic pancreatitis, IPMN	25	47%	29%	-	0%	-	-	-
Edouard Herriot Hospital, Lyon, France, 2008 (6)	1987 - 2005	50	49	Neuroendocrine tumors, serous/ mucinous cystadenoma	24	46%	8%	12%	0%	55	0%	20%
Hamburg University, Hamburg, Germany, 2010 (16)	1992 - 2007	35	60	Neuroendocrine tumors, serous/ mucinous cystadenoma	-	26%	14%	6%	0%	48	3%	0%
Columbia University, New York, USA, 2010 (10)	1997 - 2009	73	58	Serous cystadenoma, IPMN	19	41%	20%	2.7%	0%	35	14%	-
Nagoya University, Nagoya, Japan, 2010 (19)	1991 - 2006	26	58	IPMN , serous/ mucinous cystadenoma	-	38%	31%	11%	0%	71	0%	4.2%
West China Hospital, Chengdu, China, 2012 (30)	2000 - 2010	44	49	Neuroendocrine tumors, serous/ mucinous cystadenoma	34	75%	55%	-	0%	-	-	-
Beaujon Hospital, Clichy, France, 2014 (28)	2000 - 2012	100	55	Neuroendocrine tumors , IPMN	20	72%	63%	6%	3%	36	2%	7%
Fundeni Clinical Institute, Bucharest, Romania, 2015 ¹	2002 - 2014	26	35	Serous cystadenoma, neuroendocrine tumors	30	58%	38%	27%	0%	74	0%	0%

¹IPMN – intraductal papillary mucinous neoplasms; ¹Dumitrascu, unpublished data

surgical indications for this pathology, which usually has a surgical expectative approach. (31-33) A study at the Johns Hopkins University (United States) has shown that a large tumor diameter and pancreatic head location are independent risk factors for an aggressive biological behavior for a serous cystadenoma. (34) An algorithmic approach to an incidental cyst of the pancreas is associated with high rates of accurate diagnosis and management. (33)

A mucinous cystadenoma (*figure 1, a and b*) can be safely resected with a CP if the malignancy is not present or suspected. (2) The indication for resection in a mucinous cystadenoma of the pancreas is justified by the relatively high risk for malignant transformation, particularly in patients with a familial history of pancreatic cancer. (35,36)

Functional neuroendocrine pancreatic tumors such as insulinoma can be safely resected with parenchyma-sparing procedures such as CP, when a simple enucleation is not possible. (28) A recent study has shown that almost 90% of the insulinomas have a benign biological behavior, and loco-regional lymph nodes dissection appears to have no benefit. (37) An analysis of 6,222 patients resected for insulinoma has shown that the enucleation was possible in 56% of the cases, while 35% of the patients underwent a distal/ subtotal pancreatectomy. (37) Selected patients from

this latter group could potentially benefit from a CP.

For the non-functional neuroendocrine pancreatic tumors, several international guidelines recommend standard pancreatic resections, with loco-regional lymph nodes dissection, regardless the tumor size. (38) However, recent clinical data do not support the benefit of routine lymph nodes dissection in patients diagnosed with non-functional neuroendocrine pancreatic tumors. (39,40) Furthermore, few studies have shown that surgical expectative and imaging monitoring is safe in selected patients. (41) It appears that cystic pancreatic neuroendocrine tumors have a less aggressive biological behavior, compared with solid only tumors.(42) Nevertheless, several papers have shown the feasibility and oncological safety of parenchyma-sparing pancreatic resections (including CP) for non-functional pancreatic neuroendocrine tumors of the isthmus and/ or pancreatic body. (10, 28,39)

CP represents an alternative to distal pancreatectomy for selected patients with solid pseudopapillary tumors of the pancreas. (43) The widely reported benign behavior of these tumors, along with very low rates of loco-regional lymph nodes metastases justify a parenchyma-sparing approach for the solid pseudopapillary tumors of the pancreas, as recent studies have highlighted. (44-48)

Figure 1 - (a) Magnetic resonance appearance of a mucinous cystadenoma of the pancreatic isthmus – it is observed a close relationship of the tumor to the Wirsung duct (T – tumor; a white open arrow marks the Wirsung duct); (b) Central pancreatectomy for a mucinous cystadenoma – operative specimen (a white open arrow marks the tumor with the mucinous content); (c) Intraoperative aspect of a central pancreatectomy after removal of the operative specimen (a white filled arrow marks the Wirsung duct, with a small diameter); (d) Final intraoperative aspect after a central pancreatectomy (a white open arrow marks the end-to-end pancreaticojejunal anastomosis to the distal pancreatic remnant, with interrupted non-absorbable sutures); (e) Magnetic resonance appearance at 5 years after a central pancreatectomy for a pancreatic isthmus pancreatoblastoma (a filled open arrow marks the central pancreatic resection, without any recurrence) (Fundeni Clinical Institute experience, Bucharest, Romania)

Another indication for a CP is represented by the branch type intraductal papillary mucinous neoplasms. (2) The main type and the malignant branch type intraductal papillary mucinous neoplasms represent a contraindication for a parenchyma-sparing pancreatic resection, because high recurrence rates were reported. (6,8,49,50) However, good oncological outcomes were reported in several studies, for the branch type intraductal papillary mucinous neoplasms with minimally-invasive or in situ adenocarcinoma, when a margins negative resection could be accomplished. (17,51,52)

Uncommon indications for a CP are chronic pancreatitis (17,29) and pancreatic trauma. (53)

Large published series have shown that the main indications for a CP were represented by the neuroendocrine tumors (8%-36%), serous cystadenomas (20%-44%), mucinous cystadenomas (8%-35%), and branch type intraductal papillary mucinous neoplasms (12%-35%) (table 1). (6,7,9,10,16,17,19,28-30) In a recent meta-analysis, the main indications for a CP were reported to be the serous/mucinous cystadenomas (28%), followed by the neuroendocrine tumors (23%) and intraductal papillary mucinous neoplasms (18%). (2)

Beyond the benign and low malignant potential pathology, CP has been reported in several special

malignancies of the pancreas. (54,55) However, the safety of a parenchyma-sparing resection for a malignant pancreatic pathology is controversial.

A ductal adenocarcinoma of the pancreas represents an absolute contraindication for a CP, because this surgical procedure cannot provide adequate loco-regional lymph nodes dissection. (4,19,28,56) In patients with intraoperative suspected malignant pathology, a frozen section pathology examination should be performed and, if the malignancy is confirmed, a conversion to a standard distal pancreatectomy with splenectomy and lymph nodes dissection is mandatory. (1,49)

For several special malignancies such as isolated pancreatic metastases of other neoplasia and pancreatoblastoma, a CP was demonstrated to be safe and effective, in selected patients (figure 1, e). (54,55,57,58)

Most of the patients reported in the literature, resected for pancreatic metastases of other neoplasia, underwent standard pancreatic resections (59,60); however, the routine loco-regional lymph nodes dissection was not demonstrated to be of any value. (60) A standard pancreatic resection is recommended for this pathology in several centers (61), but other studies have shown the oncological safety of a parenchyma-sparing resection, when negative resection margins can be obtained. (60)

In a recent review, a CP was performed in only 1.5% of the patients resected for pancreatic metastases of other neoplasia. (59) The Memorial Sloan-Kettering Cancer Centre (United States) experience with resected pancreatic metastases of other neoplasia has shown the use of a CP in only 3% of the patients. (62) Our recent studies did not identify any significant differences of survivals between patients with CP or standard pancreatic resections for pancreatic metastases of other neoplasia, but only 16 patients with a CP were described in the literature until 2014 (Dumitrascu, unpublished data).

Iacono and co-workers have summarized the indications and contraindications of a CP. (4,21) Thus, a CP is indicated for a benign/ low malignant potential pathology or pancreatic metastases of other neoplasia, when the tumor is deeply located in the pancreatic isthmus and/ or body, and at least 5 cm of the distal remnant pancreas can be preserved. (4,21) A ductal adenocarcinoma and distal pancreatic remnant atrophy represent contraindications for a CP. (4,21)

In summary, benign and low malignant pancreatic pathology represents the largest part of indications for a CP. This pathology includes mainly serous/ mucinous cystadenoma, the branch type intraductal papillary mucinous neoplasms, solid pseudopapillary tumors, and neuroendocrine tumors. Beyond the benign pathology, selected patients with pancreatic metastases of other neoplasia might also benefit after a CP.

Technical issues in central pancreatectomy – no standard limits for resection, the fate of the distal pancreatic remnant, and the emerging role of a minimally-invasive approach

A CP is classified as non-standardized pancreatic resection (63) because there are no standard limits for resection. Thus, in a CP the amount of remnant pancreas is more important than the removed one. The limits of resection in a CP are tailored to the tumor location and pathology.

The technique of a CP has been extensively described in several papers. (4,64-69) Briefly, the middle part of the pancreas (i.e., isthmus and/ or pancreatic body) is resected, the proximal (i.e., cephalic) stump is closed (*figure 1, c*), while a digestive anastomosis is performed with the distal pancreatic stump. (4)

An open approach has been used in most of the patients reported in the literature, with a CP. (2) A minimally-invasive CP was performed in only 3% of the patients: laparoscopic approach – 1.8%, and robotic approach – 1.2%. (2) The feasibility and safety of a minimally-invasive CP were previously shown. (70,71)

In Fundeni Clinical Institute (Bucharest, Romania), the first robotic central pancreatectomy was performed in 2014, with a pancreaticogastrostomy because the pancreatic parenchyma was soft; the postoperative outcome was uneventful (Popescu, unpublished data).

Although the worldwide reported number of patients with a minimally-invasive CP is still low (only 60 cases reported until 2014), it appears that the standardization of the technique will make a significant change in the future. (70,71) Thus, in few experienced surgical centers, a minimally-invasive approach has become a standard for CP. (72) A laparoscopic approach has the potential to mitigate the invasiveness of a CP and, thus, to maximize the benefits. (73) Furthermore, a robotic approach has the potential to overcome the limitations of the conventional laparoscopy, particularly during the complex reconstructive part of a CP. (74)

Regardless the type of CP (open or minimally-invasive), the distal pancreatic remnant approach represents the most important issue, because it is the primary source of surgical morbidity. The proximal pancreatic stump is usually sutured, either manually or stapled (up to 94% of the patients) (2), while for the distal pancreatic remnant there are more options.

In an excellent review performed by Iacono and co-workers, there were described in details the technical options to treat the distal pancreatic stump. (4)

A recent review has shown that the distal pancreatic stump was sutured to the jejunum in approximately 58% of the patients with a CP (*figure 1, d*), while 38% underwent a pancreaticogastrostomy. (2) A pancreaticogastrostomy appears to be the first choice when a minimally-invasive CP is performed. (70-72,75,76)

Currently, there is no consensus regarding the best approach to the distal pancreatic remnant after a CP or a pancreaticoduodenectomy. Thus, Venara and co-workers have shown, in a single center experience, that the postoperative pancreatic fistula rate was higher when a pancreaticogastrostomy was performed. (77) The same trend was also shown in a recent meta-analysis. (2) Conversely, Xiang and co-workers have shown reduced pancreatic fistula rates after CP, when a pancreaticogastrostomy was used. (30) It is worth to mention also that recent meta-analyses of the randomized published studies associated the pancreaticogastrostomy with less overall (78-80) and severe (79) pancreatic fistula rates after pancreaticoduodenectomy, compared with the pancreaticojejunostomy, particularly in high-risk patients. (78) A previous randomized study has shown significantly less surgical complications after a pancreaticogastrostomy, compared with a pancreaticojejunostomy, in the subgroup of patients

with a soft pancreatic parenchyma. (81)

The use of a stent for the Wirsung duct during pancreaticogastro/jejunostomy is controversial. A recent meta-analysis of the randomized published studies did not show reduced pancreatic fistula rates after pancreaticoduodenectomies, in patients with internal stents. (82) However, the use of an external stent was associated with reduced overall and clinically significant pancreatic fistula rates after pancreaticoduodenectomies. (83)

An interesting approach after a CP was recently suggested by Di Benedetto and co-workers – duct-to-duct anastomosis of the Wirsung for both pancreatic remnants. (20) An internal lost stent into the duodenum was also used to protect the anastomosis. (20) The primary goal of this approach is to mitigate the consequences of a potential postoperative pancreatic fistula after a CP. (20) Thus, without any intestinal contamination, it is presumed to decrease the clinical impact of a pancreatic fistula. A similar type of reconstruction after CP was previously reported by Oida and co-workers. (84) It is worth to mention that a relatively similar approach was proposed in the first reported central pancreatic resection, more than 100 years ago. (25) However, at that time, no duct-to-duct anastomosis was performed, and the two pancreatic remnants were sutured together. (25) The feasibility of a duct-to-duct anastomosis after a CP was also shown in an experimental model. (85)

In summary, nowadays, the open CP represents the standard, but there is an emerging role for the minimally-invasive approach, which might become a standard for CP in experienced centers, particularly for the robotic approach. Currently, there is no consensus regarding the best approach to the distal pancreatic remnant; the use of either pancreaticojejunostomy or pancreaticogastrostomy is widely influenced by the surgeon expertise. However, a pancreaticogastrostomy appears to be safer, particularly when a minimally-invasive CP is preferred, or a soft pancreatic parenchyma is present. Nevertheless, an end-to-end Wirsung duct anastomosis represents a novel and interesting option in selected cases; this approach might potentially mitigate the consequences of a postoperative pancreatic fistula after CP.

Early results from central pancreatectomy – high morbidity rates, almost zero mortality

Nowadays, the morbidity after pancreatic resections remains high, despite the centralization of this surgery in experienced centers. (86)

The high morbidity rates were the main arguments

against the use of a CP. (12,13) A recent study has identified a CP as independent risk factor for early postoperative in-hospital readmission. (14) However, a national study from the United States, including 102,417 patients with pancreatic resections, has associated the distal pancreatectomies and CP with significantly less severe morbidity and mortality rates, compared with the pancreaticoduodenectomies. (86)

The overall morbidity rates after CP, reported in large series in the literature, ranged from 26% to 75%, with a postoperative pancreatic fistula as the main complication (8% to 63% of the patients) (*table 1*). (6,7,9,10,16,17,19,28-30) A recent meta-analysis has shown an overall morbidity rate of 46%, with a pancreatic fistula rate of 30% after CP. (2)

A recent review has shown that despite high rates of pancreatic fistula after a CP, most of the patients can be conservatively managed. (87) It is worth to mention that the vast variety of the morbidity and pancreatic fistula rates were strongly influenced by the definition of complications and pancreatic fistula. The use of the standardized definitions for postoperative overall (88) and specific postpancreatectomy complications (89-91) was strongly recommended for a better surgical audit.

A high postoperative pancreatic fistula rate after a CP could be explained by the two potential sources – proximal and distal pancreatic remnants (92); another explanation is the presence of a soft pancreas and a small Wirsung duct in the largest part of the patients. (6,7,9,10,16,17,19,28-30) A soft pancreatic parenchyma and a small diameter of the Wirsung duct are significant risk factors for a postoperative pancreatic fistula after all types of pancreatic resections. (93)

A feared complication after CP is severe acute postoperative pancreatitis, because it has a life-threatening potential, and sometimes require completion of the distal pancreatic remnant. In Fundeni Clinical Institute (Bucharest, Romania) experience with CP, the rate of severe acute postoperative pancreatitis was 7.8% (Dumitraşcu, unpublished data). The onset of an acute severe pancreatitis after a CP might be related to some anatomical variants of vascularization to the distal pancreas. Thus, the exclusive arterial supply of the distal pancreas along the transverse/ inferior pancreatic artery, a situation that can be encountered in up to 25% of the patients, might lead to ischemia and pancreatic necrosis. (1) The re-exploration rate for complications after CP varies between 0% and 27% in the largest worldwide published series with CP (*table 1*). (6,7,9,10,16,17,19,28-30)

A strong argument in favor of a CP is represented by the reduced mortality rates. Thus, a 0.8% mortality rate

after CP was reported in a recent meta-analysis.(2) Furthermore, except for two high-volume centers with reported mortality rates of 2.5-3% (28,29), in all other worldwide reported large series, the mortality after CP was zero (*table 1*). (6,7,9,10,16,17,19,30) It is worth to mention also that the deaths after a CP were mainly related to non-surgical causes, except for only two patients. (2,28,29) Nevertheless, the reported mortality rates after CP are by far much lower than those reported after standard pancreatic resections. Thus, a recent national study in the United States, including 21,000 standard pancreatic resections, has shown 30 days and 90 days mortality rates of 3.7% and, respectively, 7.4%. (94)

The meta-analyses comparing distal pancreatectomies with CP have shown increased overall morbidity (2,3) and pancreatic fistula rates (3) after CP. No differences between the two surgical procedures were observed for the postoperative hemorrhage, clinically relevant pancreatic fistula, re-laparotomy and mortality rates. (2,3)

Goudard and co-workers have shown in a large single center experience that a CP is associated with significant morbidity.(28) Furthermore, a careful selection of patients who might benefit after either a CP or distal pancreatectomy is suggested.(28) Thus, a pre-operative identification of patients who are at high risk to develop postoperative complications might potentially select the patients who are more likely to benefit after a CP.

Two studies have investigated potential predictors for postoperative complications after CP.(95,96) Thus, individual patient-related factors (i.e., age ≥ 40 years and a body mass index ≥ 30 kg/m²) have been identified as independent risk factors for the development of postoperative complications after a CP. (95) Furthermore, the Physiologic and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) appears to be a useful tool to predict morbidity after a CP. (96) However, the results of the above-mentioned study (96) should be regarded with caution because they might be influenced by the relatively small sample size. Recent reviews and meta-analyses have shown that POSSUM overpredicts morbidity after pancreatic resections and, thus, it has a doubtful predictive value. (97,98) Thus, at the present time there are no strong arguments to support the use of a score to predict the risk of complications after pancreatic resections, because it might jeopardize an accurate clinical decision-making. (99)

In summary, the morbidity rates after CP are high, and pancreatic fistula represents the main complication. Although the overall pancreatic fistula rates after a

CP appear to be higher, compared with the distal pancreatectomy, however, there are no significant differences in the clinically relevant pancreatic fistula rates. Identification of a subgroup of patients who are at high risk to develop complications after a CP might potentially lead to a better selection of patients who might benefit after a CP. A low mortality rate represents a strong argument in favor of a CP, in suitable patients. Finally, a selective use of a CP is recommended, in young patients, with a good biological status, which might be able to overcome the potential complications that may occur after a CP.

The impact of a central pancreatectomy on the pancreatic functions on the long-term outcome

A CP was proposed as alternative to standard pancreatic resections with the primary goal to preserve the pancreatic parenchyma and, thus, to mitigate the impact on the postoperative exocrine and endocrine functions. (1,92) A recent study has shown that the loss of a normal pancreatic tissue is significantly lower after a CP, compared with a spleen-preserving distal pancreatectomy, and, thus, there is a potential post-operatively to preserve the pancreatic functions. (100)

Preservation of the exocrine and endocrine functions is of utmost importance in patients with benign and low malignant potential pancreatic pathology because a long-term survival is expected in these patients. Thus, the quality of life in patients resected for benign pancreatic pathology should not be jeopardized on the long-term outcome. (101)

A de novo or worsening diabetes mellitus represents an important issue after pancreatic resections, and the incidence is correlated with preexisting diabetes, presence of chronic pancreatitis or pancreatic cancer, and the volume of resected pancreas. (102,103) A study has shown a 50% decrease in insulin secretion after standard pancreatectomies, with a more significant clinical impact after distal pancreatectomies. (104) Pancreatogenic diabetes mellitus is characterized by increased peripheral sensitivity to insulin and, thus, hypoglycemic episodes are more frequently encountered when the insulin is administered, sometimes with a significant clinical neurological impact. (102)

The incidence of de novo diabetes mellitus after distal pancreatectomies in patients without underlying chronic pancreatitis is reported in 7.5% to 36% of the patients. (103,104) In the largest reported series from the literature with CP, the incidence of postoperative diabetes mellitus ranges from 0% to 14% (*table 1*). (6, 7,9,10,16,17,19,28-30) Two meta-analyses have shown

that a CP is associated with significant lower rates for de novo and worsening diabetes mellitus, compared with distal pancreatectomies (5.5% vs. 23.6%). (2,3) Furthermore, the differences between the postoperative new-onset diabetes mellitus rates are more significant when a CP is compared with an extended left pancreatectomy (11% vs. 57%).(105)

Historically, the postoperative pancreatic exocrine insufficiency rates after distal pancreatectomies were reported to be of up to 61%; however, a recent study has shown almost zero pancreatic exocrine insufficiency rates after distal pancreatectomies. (106) In the largest reported series from the literature with CP, the incidence of postoperative pancreatic exocrine insufficiency rates ranges from 0% to 20% (*table 1*). (6,7,9,10,16,17, 19,28-30) Two meta-analyses have shown that a CP is associated with significant lower rates for pancreatic exocrine insufficiency, compared with the distal pancreatectomies (11.9% vs. 19.1%). (2,3)

There are also studies that have shown that, on the long-term outcome, there are no significant differences between the patients with a CP and those with a distal pancreatectomy, with respect to the nutritional status (107) or the postoperative quality of life. (101)

In summary, a CP has a minimal impact on the postoperative pancreatic functions. A de novo or worsening diabetes mellitus rates after a CP are significantly lower, compared with the distal pancreatectomies.

CONCLUSIONS

A CP can be safely incorporated into an experienced pancreatic surgeon armamentarium, albeit it represents an uncommon pancreatic resection.

Although the benign and low malignant pancreatic pathology represents the largest part of indications, however, a CP can be safely used for several particular malignancies such as pancreatic metastases of other neoplasia.

Nowadays, the open approach represents the standard, but there is an emerging role for the minimally-invasive approach, which might become a standard for CP in experienced centers, particularly for the robotic approach.

The overall morbidity and pancreatic fistula rates after CP are high, but most of the postoperative complications can be conservatively managed. A pancreaticogastrostomy appears to be safer in patients with a soft pancreatic parenchyma. A low mortality rate represents a strong argument in favor of a CP.

Tumors located in the pancreatic isthmus are more likely to benefit after a CP, because in these patients an

alternative left extended pancreatectomy should be performed, with a high potential for an adverse impact on the pancreatic functions.

A selective use of a CP is recommended, in young patients, non-obese and without diabetes mellitus, with a good biological status, which might be able to overcome the potential complications that may post-operatively occur.

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