

CONFERENCE REPORT

Medical Complications of Pancreatic Resections

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Summary

The sequelae of pancreas surgery are determined by the type of procedure, the extent of the parenchymal resection and the underlying disorder. In ductal carcinoma, the outcome is heavily influenced by the disease itself. Mortality rates are lower in centers which perform the most operations.

In chronic pancreatitis, surgical management is essentially therapeutic for complications and palliative for the disease whose progress is closely correlated with the sequelae.

Elective surgery does not appear to increase the risk of diabetes whereas distal pancreatectomy is an independent risk factor. Parenchymal resection aggravates nutritional deficiencies, such as low selenium, linoleic acid, LDL and apolipoprotein B levels, and thus increases the risk of atherogenesis. Abstinence from alcohol is an indispensable step towards the disappearance of postoperative pain.

The sequelae of pancreas surgery are determined by the type of procedure (resective or derivative), the extent of the parenchymal resection, and the underlying disorder. The literature is rich in data regarding the outcome of resection in the management of neoplastic lesions. In ductal carcinoma, the outcome is heavily influenced by the disease itself. Morbidity associated with resection of the pancreatic head is relatively high (up to 60%), and there is no

statistically significant difference between classic partial and pylorus-preserving pancreaticoduodenectomy [1].

Numerous studies have reported a promising increase in 5-year survival when ductal carcinoma surgery is followed by radiotherapy and chemotherapy [2, 3, 4]. It has also been shown that mortality rates are lower in centers which perform the most operations [5]. In this connection, of course, it must be borne in mind that specialized centers employ more sophisticated means of diagnosis. They are also furnished with appropriate intensive care units and usually have access to more abundant resources.

Chronic pancreatitis is a benign disorder. Progressive, persistent destruction of the pancreas may remain silent for years until the onset of serious insufficiency or it may appear in the form of irregular and painful acute episodes or complications. The prime indications for surgery are uncontrolled pain or complications (e.g., pseudocysts). Elimination of the cause of the disease (alcohol, obstruction, autoimmunity) improves or abolishes recrudescences, but does not result in a cure. As has already been stated, in fact, chronic pancreatitis progresses to the point of insufficiency, which means that surgical management is essentially therapeutic for complications and palliative for the disease.

Genes involved in trypsinogen instability are thought to be responsible for pancreatitis [6, 7, 8, 9, 10]. Enhanced trypsinogen activation in the exocrine cells may increase their

apoptosis and turnover, and hence cause exocrine insufficiency and parenchymal fibrosis (painless pancreatitis), or massive activation followed by recrudescence and necrosis. The genetic substrate of other, more numerous situations has not been determined and environmental factors, such as alcohol and a high-fat diet, are the only known causes.

In a family described in a personal study [11], a cationic trypsinogen mutation in exon 2 (V39A) was responsible for serious, clinically silent pancreatitis which led to insufficiency and required resective/derivative surgery due to the appearance of a tumor or severe complications.

Surgery is indicated in cases of chronic pancreatitis for the resolution of complications (especially intractable pain) or when differentiation of tumors is uncertain.

Morbidity following resection of the pancreatic head combined with longitudinal pancreaticojejunostomy (Frey procedure) and duodenum-preserving head resection (Beger procedure) is 39% (compared with 48% for other resections), with a 20% revision rate in both cases [12, 13, 14].

Long-term mortality is 32% after both the Frey and the Beger procedures [15]. Falconi *et al.*, however, achieved better results with no mortality and significant reduction of pain in a series of 40 patients operated on according to Frey [16].

Abstinence from alcohol is an indispensable step towards the disappearance of postoperative pain [14]. The quality of life of patients with pancreatitis is significantly worse than that of the controls, mainly due to pain [17]. Reason would suggest that reduction of the parenchyma or better drainage of the ducts would be sufficient to reduce recrudescence. This has not yet been established in controlled long-term trials.

The sequelae of surgery may aggravate the clinical course (Table 1). The incidence of diabetes after resection is closely correlated with the surgical procedure: 25-40% after Whipple; 8-15% after Frey; about 60% five years after distal pancreatectomy due to the greater concentration of islet cells in the tail.

Elective surgery does not appear to increase the risk of diabetes, whereas distal pancreatectomy is an independent risk factor. Long-term postoperative mortality increases if alcohol is not eliminated [15]. Alcohol and diabetic decompensation are the main factors responsible for high long-term postoperative mortality [18].

Exocrine insufficiency is directly correlated with the type of pancreatitis and serious insufficiency is directly correlated with the disappearance of pain ("burn out") [19]. The incidence of exocrine deficiency ranges from 35% to 74% in function of the type of resection [13]. These clinical considerations must be borne in mind when weighing up the efficacy of surgery as a remedy for pain in chronic pancreatitis.

Resection also aggravates secondary nutritional deficiencies, such as low selenium, linoleic acid, LDL and apolipoprotein B levels, and thus increases the risk of atherogenesis. Cardiovascular complications are frequent in chronic pancreatitis and are further aggravated by glycemic decompensation [20, 21].

The enhanced risk of both extrapancreatic [22] and pancreatic [23] neoplasias is an important factor in the long-term management of patients with chronic pancreatitis.

In hereditary forms due to cationic trypsinogen gene mutations, its frequency is 50% at age 50 and 70% at age 65 and older [24].

In conclusion, the sequelae of surgery are closely correlated with the progress of chronic pancreatitis. They primarily take the form of exocrine insufficiency, nutritional deficiencies, diabetes and its complications,

Table 1. Medical complications of chronic pancreatitis.

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- Exocrine insufficiency
 - Diabetes
 - Autonomic neuropathy
 - Intestinal malabsorption
 - Intestinal bacterial pollution
 - Atherosclerosis
 - Bone changes
 - Pancreatic carcinoma
 - Extraprostatic carcinoma
 - Psychosis
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altered lipid metabolism with an increased risk of atherogenesis, and both extrapancreatic and pancreatic carcinoma.

Keywords Diabetes Mellitus; Exocrine Pancreatic Insufficiency; Pancreas /surgery; Pancreatitis, Chronic; Postoperative Complications

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References

1. Schniewind B, Bestmann B, Henne-Bruns D, Faendrich F, Kremer B, Kuechler T. Quality of life after pancreaticoduodenectomy for ductal adenocarcinoma of the pancreatic head. *Br J Surg* 2006; 93:1099-107. [PMID 16779883]
2. Reni M, Passoni P, Bonetto E, Balzano G, Panucci MG, Zerbi A, et al. Final results of a prospective trial of a PEFG (Cisplatin, Epirubicin, 5-Fluorouracil, Gemcitabine) regimen followed by radiotherapy after curative surgery for pancreatic adenocarcinoma. *Oncology* 2005; 68(2-3):239-45. [PMID 16015040]
3. Chua YJ, Cunningham D. Adjuvant treatment for resectable pancreatic cancer. *J Clin Oncol* 2005; 23:4532-7. [PMID 16002844]
4. Neoptolemos JP, Baker P, Beger H, Link K, Pederzoli P, Bassi C, et al. Progress report. A randomized multicenter European study comparing adjuvant radiotherapy, 6-mo chemotherapy, and combination therapy vs no-adjuvant treatment in resectable pancreatic cancer (ESPAC-1). *Int J Pancreatol* 1997; 21:97-104. [PMID 9209950]
5. Evans JD, Wilson PG, Carver C, Bramhall SR, Buckels JA, Mayer AD, et al. Outcome of surgery for chronic pancreatitis. *Br J Surg* 1997; 84:624-9. [PMID 9171747]
6. Cohn JA, Friedman KJ, Noone PG, Knowles MR, Silverman LM, Jowell PS. Relation between mutations of the cystic fibrosis gene and idiopathic pancreatitis. *N Engl J Med* 1998; 339:653-8. [PMID 9725922]
7. Sharer N, Schwarz M, Malone G, Howarth A, Painter J, Super M, Braganza J. Mutations of the cystic fibrosis gene in patients with chronic pancreatitis. *N Engl J Med* 1998; 339:645-52. [PMID 9725921]
8. Arduino C, Gaia E. Genetics of chronic pancreatitis. *Biomed Pharmacother* 2000; 54:394-9. [PMID 10989979]
9. Gorry MC, Ghabbaizadeh D, Furey W, Gates LK Jr, Preston RA, Aston CE, et al. Mutations in the cationic trypsinogen gene are associated with recurrent acute and chronic pancreatitis. *Gastroenterology* 1997; 113:1063-8. [PMID 9322498]
10. Witt H, Luck W, Hennies HC, Classen M, Kage A, Lass U, et al. Mutations in the gene encoding the serine protease inhibitor, Kazal type 1 are associated with chronic pancreatitis. *Nat Genet* 2000; 25:213-6. [PMID 10835640]
11. Arduino C, Salacone P, Pasini B, Brusco A, Salmin P, Bacillo E, et al. Association of a new cationic trypsinogen gene mutation (V39A) with chronic pancreatitis in an Italian family. *Gut* 2005; 54:1663-4. [PMID 16227369]
12. Sohn TA, Campbell KA, Pitt HA, Sauter PK, Coleman JA, Lillemo KD, et al. Quality of life and long-term survival after surgery for chronic pancreatitis. *J Gastroenterol Surg* 2000; 4:355-64. [PMID 11058853]
13. Frey CF, Mayer KL. Comparison of local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy (Frey procedure) and duodenum-preserving resection of the pancreatic head (Beger procedure). *World J Surg* 2003; 27:1217-30. [PMID 14534822]
14. Belina F, Fronck J, Ryska M. Duodenopancreatectomy versus duodenum-preserving pancreatic head excision for chronic pancreatitis. *Pancreatol* 2005; 5:547-52. [PMID 16110253]
15. Strate T, Taherpour Z, Bloechle C, Mann O, Bruhn JP, Schneider C, Kuechler T, Yekebas E, Izbicki JR. Long-term follow-up of a randomized trial comparing the beger and frey procedures for patients suffering from chronic pancreatitis. *Ann Surg* 2005; 241:591-8. [PMID 15798460]
16. Falconi M, Bassi C, Casetti L, Mantovani W, Mascetta G, Sartori N, et al. Long-term results of Frey's procedure for chronic pancreatitis: a longitudinal prospective study on 40 patients. *J Gastrointest Surg* 2006; 10:504-10. [PMID 16627215]
17. Pezzilli R, Bini L, Fantini L, Baroni E, Campana D, Tomassetti P, Corinaldesi R. Quality of life in

chronic pancreatitis. *World J Gastroenterol* 2006; 12:6249-51. [PMID 17072944]

18. Olah A, Kelemen D, Horvath OP, Belagyi T. Long-term follow-up results of surgery for chronic pancreatitis. *Hepatogastroenterology* 2004; 51:1179-82. [PMID 15239273]

19. Ammann RW. Diagnosis and management of chronic pancreatitis: current knowledge. *Swiss Med Wkly* 2006; 136:166-74. [PMID 16633964]

20. Quilliot D, Walters E, Guerci B, Fruchart JC, Duriez P, Drouin P, Ziegler O. Effect of the inflammation, chronic hyperglycemia, or malabsorption on the apolipoprotein A-IV concentration in type 1 diabetes mellitus and in diabetes secondary to chronic pancreatitis. *Metabolism* 2001; 50:1019-24. [PMID 11555832]

21. Petrin P, Chiappetta A, Del Favero G, Farini R, Pedrazzoli S. Chronic pancreatitis and diabetes. *Minerva Med* 1983; 74:31-8. [PMID 6337349]

22. Rocca G, Gaia E, Iuliano R, Caselle MT, Rocca N, Calcamuggi G, Emanuelli G. Increased incidence of cancer in chronic pancreatitis. *J Clin Gastroenterol* 1987; 9:175-9. [PMID 3571892]

23. Talamini G, Falconi M, Bassi C, Sartori N, Salvia R, Caldiron E, et al. Incidence of cancer in the course of chronic pancreatitis. *Am J Gastroenterol* 1999; 94:1253-60. [PMID 10235203]

24. Howes N, Lerch MM, Greenhalf W, Stocken DD, Ellis I, Simon P, et al. Clinical and genetic characteristics of hereditary pancreatitis in Europe. *Clin Gastroenterol Hepatol* 2004; 2:252-61. [PMID 15017610]