Diabetul zaharat post-rezectie pancreatica, preventie si atitudine
The number of patients undergoing pancreatic surgery is increasing:

- Early diagnosis of premalignant lesions
- Referral of patients affected by surgical pancreatic disease to high-volume centers.\(^1,2\)

Life expectancy of patients undergoing pancreatectomy has increased in recent years

**Post-resection diabetes** is now attracting attention as a factor influencing quality of life and life expectancy of patients who have undergone this procedure

Classification of Diabetes

- **Type 1 diabetes**
  - β-cell destruction
- **Type 2 diabetes**
  - Progressive insulin secretory defect
- **Other specific types of diabetes**
  - Genetic defects in β-cell function, insulin action
  - Diseases of the exocrine pancreas
  - Drug- or chemical-induced
- **Gestational diabetes mellitus (GDM)**
Review article

Diabetes mellitus secondary to pancreatic diseases (Type 3c) — Are we neglecting an important disease?

Nils Ewald *, Reinhard G. Bretzel

Pancreatogenic, pancreoprive or apancreatic diabetes mellitus is classified as a form (type 3c) of secondary or type 3 diabetes mellitus (T3cDM) by the American Diabetes Association and by the World Health Organization [1,3]. Exocrine pancreatic diseases underlying T3cDM include benign and malign conditions such as acute, relapsing and chronic pancreatitis of any etiology, hemochromatosis, cystic fibrosis, fibrocalculus pancreatopathy, pancreatic trauma, pancreatectomy, pancreatic agenesis and pancreatic cancer [1,3,4]. Yet, the most common underlying disease seems to be chronic pancreatitis.
2-3 % of the type 3c DM are patients who underwent pancreatectomy\textsuperscript{1, 2}

\textsuperscript{1}Ewald N et al. Diabetes Met Res Rev. 2011;28: 338-42
\textsuperscript{2}Hardt PB e al. Diab. Care 2008; 31 Suppl 2: S165-169
Definitions of post-pancreatic resection DM

• postoperative “new-onset DM”:
  – FPG > 126 mg/dl detected on two or more separate days
  – Plasma glucose > 200 mg/dl measured in 2 h after a 75 g glucose drink

• “late-onset diabetes” (later than 3 months after surgery)
Clinical and laboratory character in type 3c DM

In patients with Type 3c DM due to pancreatectomy was reported a mean of 8.1\% HbA1c, which was not statistically significant from the entire diabetic populations.


<table>
<thead>
<tr>
<th>Parameter</th>
<th>Type 1 IDDM juvenile onset</th>
<th>Type 2 NIDDM adult onset</th>
<th>Type 3c pancreateogenic postop. onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoacidosis</td>
<td>common</td>
<td>rare</td>
<td>rare</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>severe</td>
<td>usually mild</td>
<td>mild</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>common</td>
<td>rare</td>
<td>common</td>
</tr>
<tr>
<td>Peripheral insulin sensitivity</td>
<td>normal or increased</td>
<td>decreased</td>
<td>increased</td>
</tr>
<tr>
<td>Hepatic insulin sensitivity</td>
<td>normal</td>
<td>normal or decreased</td>
<td>decreased</td>
</tr>
<tr>
<td>Insulin levels</td>
<td>low</td>
<td>high</td>
<td>low</td>
</tr>
<tr>
<td>Glucagon levels</td>
<td>normal or high</td>
<td>normal or high</td>
<td>low</td>
</tr>
<tr>
<td>PP levels</td>
<td>normal or low (late)</td>
<td>high</td>
<td>low</td>
</tr>
<tr>
<td>GIP levels</td>
<td>normal or low</td>
<td>normal or high</td>
<td>normal or high</td>
</tr>
<tr>
<td>GLP-1 levels</td>
<td>normal</td>
<td>normal or high</td>
<td>normal or high</td>
</tr>
<tr>
<td>Typical age of onset</td>
<td>childhood or adolescence</td>
<td>adulthood</td>
<td>any</td>
</tr>
</tbody>
</table>
The etiology of Post-resection DM

- Recurrence or progression of underlying disease (reduction of the islet cell reserve)
- Gland atrophy
- Adjuvant chemotherapy or radiation
- The type of surgery:
  - Extend of the resection (volume of resection) – loss of pancreatic parenchyma
  - Neurohormonal response after resection
Post-resection DM- incidence ranging from 0% to 50%\textsuperscript{3}

- **4.8 to 38\%** of patients after DP (distal pancreatectomy)
- **20\%** of the patients after pancreaticoduodenectomy
Pancreatogenic Diabetes after Pancreatic Resection

Hiromichi Maeda\textsuperscript{a, b} Kazuhiro Hanazaki\textsuperscript{a}

**Table 1. Incidence of postoperative diabetes mellitus**

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Authors</th>
<th>Patients</th>
<th>Pathology</th>
<th>NO-DM</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DP</td>
<td>Hutchins et al. [7]</td>
<td>90</td>
<td>chronic pancreatitis</td>
<td>32/77 (42%)</td>
<td>34 months (mean)</td>
</tr>
<tr>
<td></td>
<td>Schoenberg et al. [10]</td>
<td>74</td>
<td>chronic pancreatitis</td>
<td>16/58 (28%)</td>
<td>58 months (median)</td>
</tr>
<tr>
<td></td>
<td>Lillemoe et al. [13]</td>
<td>235</td>
<td>24% chronic pancreatitis 76% tumors</td>
<td>19/235 (8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>King et al. [14]</td>
<td>125</td>
<td>8.8% chronic pancreatitis 92% tumors</td>
<td>10/111 (9%)</td>
<td>21 months (median)</td>
</tr>
<tr>
<td></td>
<td>Shoup et al. [15]</td>
<td>211</td>
<td>tumors</td>
<td>6/211 (5%)</td>
<td>21 months (median)</td>
</tr>
<tr>
<td>CP</td>
<td>Adham et al. [22]</td>
<td>50</td>
<td>tumors</td>
<td>0/19 (0%)</td>
<td>55 months (median)</td>
</tr>
<tr>
<td></td>
<td>Allendorf et al. [23]</td>
<td>26</td>
<td>benign tumors</td>
<td>2/26 (8%)</td>
<td>33 months (mean)</td>
</tr>
<tr>
<td></td>
<td>Sudo et al. [24]</td>
<td>19</td>
<td>benign tumors</td>
<td>0/19 (0%)</td>
<td>71 months (median)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPPHR</td>
<td>Keck et al. [28]</td>
<td>92</td>
<td>chronic pancreatitis</td>
<td>34%/14% (Frey/Beger)</td>
<td>60 months (median)</td>
</tr>
<tr>
<td>PD</td>
<td>Traverso and Kozarek [29]</td>
<td>57</td>
<td>chronic pancreatitis</td>
<td>18/57 (32%)</td>
<td>42 months (mean)</td>
</tr>
<tr>
<td></td>
<td>Sakorafas et al. [31]</td>
<td>105</td>
<td>chronic pancreatitis</td>
<td>48%*</td>
<td>6.6 years (mean)</td>
</tr>
<tr>
<td></td>
<td>Huang et al. [32]</td>
<td>103</td>
<td>48% benign tumors</td>
<td>13/49 (27%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Falconi et al. [33]</td>
<td>51</td>
<td>52% pancreatic cancer benign tumors</td>
<td>21/54 (39%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Müller et al. [8]</td>
<td>147</td>
<td>various</td>
<td>147/147 (100%)</td>
<td>not defined</td>
</tr>
</tbody>
</table>

NO-DM = New-onset diabetes mellitus; DP = distal pancreatectomy; CP = central pancreatectomy; DPPHR = duodenum-preserving pancreatic head resection; PD = pancreaticoduodenectomy; TP = total pancreatectomy.

* Preoperative evaluation identified diabetes in 8% of patients.
# Pancreatic Resection: Effects on Glucose Metabolism

Lori A. Slezak, M.D., Dana K. Andersen, M.D.

## Table 2. Various pancreatic resections with incidence of postoperative diabetes.

<table>
<thead>
<tr>
<th>Procedure (% resection)</th>
<th>Proph DM → postop DM</th>
<th>Rx of postop DM</th>
<th>Mortality (%)</th>
<th>Other postop findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreaticoduodenectomy (50%)</td>
<td>15% 26% [11]</td>
<td>60% Diet or oral hypoglycemics</td>
<td>0.6 [14]</td>
<td>PP deficient with hepatic insulin resistance</td>
</tr>
<tr>
<td>All glucose-intolerant [10]</td>
<td></td>
<td></td>
<td>8.2 [8]</td>
<td></td>
</tr>
<tr>
<td>Pylorus-preserving pancreaticoduodenectomy (50%)</td>
<td>27% IDDM 37% IDDM</td>
<td>0 [4, 15]</td>
<td>Insulin secretion capacity, glucagon secretion capacity [4] PP deficient with hepatic insulin resistance</td>
<td></td>
</tr>
<tr>
<td>40% IOGTT 40% IOGTT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33% Normal 23% Normal [15]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All glucose-intolerant postop [4]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40% IOGTT 45% IOGTT [16]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15% Normal 10% Normal [17]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Normal glucose tolerance postop [4]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.4% Incidence new-onset IDDM [18]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenum-preserving pancreatic head resection/Frey procedure (15%)</td>
<td>36% IDDM 36% IDDM</td>
<td>0–3.2 [15, 17]</td>
<td>Postop morbidity 9% [17]</td>
<td></td>
</tr>
<tr>
<td>46% IOGTT 50% IOGTT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18% Normal 14% Normal [17]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IOGTT: impaired oral glucose tolerance; OGT: oral glucose tolerance; DM: diabetes mellitus; Rx: treatment.
PRV= \( \frac{\text{resected volume of normal pancreas}}{\text{total volume of normal pancreas}} \times 100 \)
The volume reduction of the pancreatic parenchyma—risk factor for diabetes

The mean PRV for the new-onset group was 49% vs 32% for the non-diabetic group

PRV >44%- independent risk factor for postoperative new onset diabetes

Using the PRV—offer specific information about individual risk of the postoperative DM
Human pancreas imaging.


http://www.plosone.org/article/info:doi/10.1371/journal.pone.0055991
PANCREATIC CANCER (PDAC) AND DM
Incidence of DM after pancreatic resection in PDAC

1. Distal pancreatectomy
   - Between **40% to 80%** of the pancreas is removed, depending on the indication for surgery (location of the tumor)\(^1,2\)
   - The rate of new-onset DM after DP in patients with remaining normal parenchyma is low compared with CP - **5-9%**\(^3\)

---
2. Pancreaticoduodenectomy (PD)

- The rate of new-onset DM after PD in patients with PDAC
- Amelioration of the diabetes state has been often observed after PD for PDAC
Resolution of New-Onset Diabetes After Radical Pancreatic Resection Predicts Long-term Survival in Patients with Pancreatic Ductal Cell Adenocarcinoma

Xiang Yi He et al. suggests that nearly half of newly diagnosed PDAC patients have DM.

71.1% of these patients have new-onset DM (≤2 years) and

65% of new-onset DM are resolved post-radical resection.
Resolution of New-Onset Diabetes After Radical Pancreatic Resection Predicts Long-term Survival in Patients with Pancreatic Ductal Cell Adenocarcinoma

The mechanisms responsible for resolution of DM:
- Surgical resection- associated anatomical changes

Local effects: removal of the:
- diabetogenic factors secreted by the adenocarcinoma cells
- local inflammation due to obstructive lesions (cause insuline resistance)

The effect of preoperative DM on pancreatic fistula is controversial

Mathur et al. – DM offer a protective benefit against pancreatic fistula

- The patients developed pancreatic fistula were less likely to have diabetes. (p<0.05)

1,2 Mathur A. Et al. 2007 Ann Surg.
Postoperative outcome after pancreatectomy in patients with **preoperative DM**

- Pre-existing DM may have prognostic implications after resection for PDAC\(^1,2\)

- Patients with preoperative DM – higher risk of any type of pancreatic fistula than those without DM (10.3% vs 3.7%)

- The risk for ISGAPS type B and C is similar (\(p=0.8\))

- No significant difference in the rate of postoperative mortalities between two groups


Pre-operative DM, tumor size > 2 cm, lymph node ratio (LNR)> 0.1, and positive resection margin were associated with a poorer DFS and OS.
SOLUTION FOR MANAGEMENT
Management of the

1. Glycemic control

1. Treatment of additional comorbidities (maldigestion, qualitative malnutrition)
Total Pancreatectomy With Islet Autotransplantation in Patients With Malignancy

Are We There Yet?

Vikas Dudeja, MD, Greg J. Beilman, MD, and Selwyn M. Vickers, MD

Annals of Surgery • Volume 258, Number 2, August 2013

Exclusion criteria for TPIAT at University of Minnesota

III. Contraindications

1. Active alcoholism (patient must be abstinent for 6 mo with documented success of therapy)
2. Pancreatic cancer
3. End-stage pulmonary disease, cirrhosis, or severe ASHD
4. Poorly controlled psychiatric illness
5. Inability to comply with postoperative regimen
6. Patients with IPMN should not receive islet cell autotransplant outside of clinical trial
7. Illegal drug usage (patient must be abstinent for 6 mo with documented success of therapy)
Why malignancy or concern for malignancy remains a clear exclusion for TPIAT?

Concern for the use of islet preparation contaminated with ductal cells in patients with malignancy

- The islet isolation process enriches islets, but does not totally eliminate ductal cells (cell of origin for pancreatic ductal adenocarcinoma)

- Multifocality has been described in pancreatic cancer
BENIGN AND LOW GRADE MALIGNANT LESIONS AND DM
What is chronic pancreatitis?

- Chronic pancreatitis is a progressive inflammatory disease implying destroyed secretory pancreatic parenchyma and replacement with fibrous tissue, that could lead to both exocrine and endocrine insufficiency (i.e. malnutrition and diabetes)

*Braganza JM, Lancet, 2011*
Treatment goals

• Relieve pain / prevent recurrent attacks

• Manage complications

• Correct metabolic consequences such as diabetes or malnutrition
Surgical treatment of chronic pancreatitis - a 14 years experience

C. Stroescu, S. Dima, A. Scarlat, B. Ivanov, O. Bouaru, M. Ionescu, C. Vasilescu, I. Popescu
Centrul de Chirurgie Generală și Transplant Hepatic, Institutul de Boli Digestive și Transplant Hepatic Fundeni, București


Resection procedures: 150 between 1995 and 2008

Whipple procedure - 72 patients
Pylorus preserving PD - 24 patients
Duodenum preserving pancreatic head resections in 10 patients
  • Beger procedure - 6 patients
  • Frey procedure – 4 patients
Distal pancreatectomy
  • with splenectomy - 38 patients
  • spleen preserving - 4 patients
Total pancreatectomy - 2 patients
DM after pancreatic resection in **CP-Distal pancreatectomy**

- For patients with **CP** the incidence of **post-resection DM** may reflect the underlying disease progression in addition to the effects of resection. \(^1\)
- **25-50%** of patients with **CP** have risk of developing **DM after DP**\(^2\)

\(^1\) Ferrara M et al. CHBP 2013, 15: 170-174

\(^2\) Maeda H, Hanazaki K. Pancreatology 2011; 11:268-276
DM after pancreatic resection in **CP-proximal pancreatectomy**

DPPHR and PD seem to be equally effective in terms of postoperative pain relief, overall morbidity, and incidence of postoperative endocrine insufficiency. However, the data suggest superiority of DPPHR in the treatment of chronic pancreatitis with regard to several peri and postoperative outcome parameters and quality of life. Further RCTs are eagerly awaited to prove these findings.

*Diener MK, Ann Surg, 2008*
DM after pancreatic resection in CP-Distal pancreatectomy

- Büchler et al. compared endocrine function following pylorus preserving partial pancreaticoduodenectomy or duodenum-preserving pancreatic head resection (DPPHR, or “Beger” procedure) performed for chronic pancreatitis.

The observation that the DPPHR (Beger) procedure was superior to pylorus-preserving pancreaticoduodenectomy with respect to glucose metabolism suggests that preservation of the duodenum (or the pancreatic polypeptide- and insulin-containing tissue in the ventral pancreas) was responsible for improved glucose tolerance postoperatively.

Total / near-total pancreatectomy

- Extensive / demanding surgery
- Severe metabolic consequences - IDDM

Chronic pancreatitis
(up to 83% within 25 years of the clinical onset)

Pancreatogenic diabetes

- Frequently hypoglycemic attacks - severe 41%
  - Hospitalization
  - Central nervous system damage / death
  - Glycemic control - challenging

Specialized and distinct management

Pancreatic enzymes - 97%
Severe diarrhoea - 18%
Microvascular complication - 23%

Cui YF, Pancreatology, 2011; Maeda H, Pancreatology, 2011; Parsaik AK, Clinical Endocrinology, 2010
Total pancreatectomy should no longer be generally avoided, because it is a viable option in selected patients.


Mortality decreased from 22% to 3%, but hypoglycemia continues to be a problem.
Duodenum- and spleen-preserving total pancreatectomy for end-stage chronic pancreatitis

N. Alexakis, P. Ghaneh, S. Connor, M. Raraty, R. Sutton and J. P. Neoptolemos

Table 1 Results of total pancreatectomy for chronic pancreatitis in series with at least ten patients with follow-up since 1987

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>No. of patients</th>
<th>Operation</th>
<th>Hospital morbidity</th>
<th>Postoperative deaths</th>
<th>Patients with complete pain relief* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper et al.31†</td>
<td>1987</td>
<td>83</td>
<td>TP, DpTP</td>
<td>—</td>
<td>4 (4.8)</td>
<td>83</td>
</tr>
<tr>
<td>Linehan et al.32</td>
<td>1988</td>
<td>29</td>
<td>TP, DpTP</td>
<td>18 (62.1)</td>
<td>1 (3.4)</td>
<td>80</td>
</tr>
<tr>
<td>Fleming and Williamson10</td>
<td>1995</td>
<td>40</td>
<td>TP, DpTP, SpTP</td>
<td>15 (37.5)</td>
<td>2 (5.0)</td>
<td>79</td>
</tr>
<tr>
<td>Sakorafas et al.33</td>
<td>2000</td>
<td>19</td>
<td>TP</td>
<td>9 (47.4)</td>
<td>1 (5.3)</td>
<td>75</td>
</tr>
<tr>
<td>White et al.15</td>
<td>2000</td>
<td>35</td>
<td>SpTP, TP</td>
<td>15 (42.9)</td>
<td>1 (2.9)</td>
<td>83</td>
</tr>
<tr>
<td>Present series</td>
<td>2003</td>
<td>19</td>
<td>DpSpTP</td>
<td>5 (26.3)</td>
<td>1 (5.3)</td>
<td>81</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. *Variable follow-up; †multi-centre study; TP, total pancreatectomy; DpTP, duodenum-preserving total pancreatectomy; SpTP, spleen-preserving total pancreatectomy; DpSpTP, duodenum- and spleen-preserving total pancreatectomy.
DC, 29 yrs old, idiopathic chronic pancreatitis progressively affecting the whole pancreas (2001)

Resistant pain to medical and non-resectional surgical treatment (left thoracoscopic splanchnicectomy) (April 2007)

CA 19-9 tumor marker reaches values over 100 U/mL.

Follow-up- good regarding pain control diabetes control - 32 Ul Insulin

SOLUTION FOR MANAGEMENT

- Parenchyma sparing procedures
- Islet autotransplantation
Parenchyma sparing surgery

Central pancreatectomy
CP removes only central lesions and preserves a greater volume of pancreatic tissue.

The incidence of the endocrine failure was 5.5% after CP and 23.6% after DP.
Central Pancreatectomy versus Spleen-Preserving Distal Pancreatectomy: A Comparative Analysis of Early and Late Postoperative Outcomes

Traian Dumitrascu  Andra Scarlat  Mihnea Ionescu  Irinel Popescu
Center of General Surgery and Liver Transplant, Fundeni Clinical Institute, Bucharest, Romania

Table 3. Comparative analysis of pathology data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CP (n = 22)</th>
<th>SPDP (n = 25)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign</strong></td>
<td></td>
<td></td>
<td>1²</td>
</tr>
<tr>
<td>Insulinoma</td>
<td>2 (6%)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>9</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>Borderline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroendocrine neoplasia G1</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Solid pseudo-papillary tumor</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Intraductal mucinous papillary tumor, branch type</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Malignant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastases of other neoplasm</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pancreatoblastoma</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Neuroendocrine neoplasia G2/G3</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Osteoclast-like carcinoma</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cystadenocarcinoma</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lesion size, cm³</td>
<td>3 (1.5–14)</td>
<td>4 (0.4–14)</td>
<td>0.465³</td>
</tr>
<tr>
<td>Length of resected pancreas, cm²</td>
<td>5 (4–9)</td>
<td>8.5 (6–12)</td>
<td>&lt;0.001³</td>
</tr>
</tbody>
</table>

Table 5. Comparative analysis of long-term outcome

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CP (n = 20)</th>
<th>SPDP (n = 23)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, months¹</td>
<td>59 (7–122)</td>
<td>47 (4–104)</td>
<td>0.287²</td>
</tr>
<tr>
<td>New-onset/worsening diabetes n</td>
<td>0</td>
<td>4 (16%)</td>
<td>0.111³</td>
</tr>
<tr>
<td>Exocrine pancreatic insufficiency, n</td>
<td>0</td>
<td>1 (4%)</td>
<td>1³</td>
</tr>
<tr>
<td>Late complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(incisional hernia), n</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td>1³</td>
</tr>
<tr>
<td>Recurrence of disease, n</td>
<td>2 (8%)</td>
<td>4 (16%)</td>
<td>0.670³</td>
</tr>
</tbody>
</table>

¹ Range in parentheses.
² Log-rank test.
³ Fisher’s exact test (two-tailed).
Chronic pancreatitis - total pancreatectomy and autologous islet transplants
1. Glycemic control
2. Treatment of additional comorbidities (maldigestion, qualitative malnutrition)
   - risk of vitamin D deficiency (risk of osteoporosis)
   - risk of impaired incretin secretion (pancreatic enzyme replacement)
3. Cancer risk
   - Use of the Metformin may be beneficial
     CP and T3c DM are risk factors for the development of pancreatic cancer
Transplantation of Native Islets for Patients with Pancreatitis

Isolated Native Islet of Langerhans

Islet Isolation

Syringe

Pancreas

Liver

Patient with Pancreatitis

Marquez S, Pancreas, 2010
Islet autotransplantation

TABLE 1. Indications and Contraindications for TPIAT
“Minnesota Criteria”

To be considered for TPIAT, patients must meet criteria in sections I and II and have no contraindications:

I. Definitions (must have A, B, or C)

A. CP (must have one of 1, 2, or 3)

Patients with chronic abdominal pain, lasting >6 mo, features consistent with that of pancreatitis, and evidence of CP as evidenced by at least one of the following:

1. Morphologic/functional evidence of CP [CT of abdomen with evidence of CP (calcifications), or ERCP evidence of pancreatitis]

2. EUS of ≥6/9 criteria positive for CP

or

3. At least 2 of the following 3 findings:
   i. Secretin MRCP or ERCP, with findings suggestive of CP (abnormal duct/side branch) or MRI T2 evidence of fibrosis
   ii. EUS with ≥4/9 criteria positive for pancreatitis
   iii. Abnormal exocrine pancreatic function tests (peak bicarbonate <80)

or

B. Relapsing AP (must have both 1 and 2)

1. Three or more episodes of documented AP with ongoing episodes over >6 mo.

2. No evidence of current gallstone disease or other correctible etiology such as autoimmune pancreatitis

or

C. Documented hereditary pancreatitis with compatible clinical history.
Total pancreatectomy technique

Islet cells - reduced warm ischemia - preserve blood supply - increase islet yield


Duodenum and spleen preserving total pancreatectomy and islet autotransplantation

MJ, 53 yrs old, chronic pancreatitis affecting the whole pancreas
Islet cells infusion

3 techniques:

• Patient with open abdomen in OR
  - The most common method

• PO percutaneous transhepatic approach
  - Safe and more cost-effective
    (Morgan KA, HPB, 2011)

• IOP placement of a catheter

Farnell MB, HPB, 2011

Nath DS, J Am Coll Surg, 2004
Results of total pancreatectomy and autoislet transplant

- **Complications:** 6% to 42%
  - Ris F, Transplantation, 2011; Morgan KA, HPB, 2011; Desai CS, J Am Coll Surg, 2011

- **Insulin independence:**
  - at 1 year: 47% - 95%
    - Ris F, Transplantation, 2011; Sutherland DER, Transplantation, 2008; Wahoff SC, Ann Surg, 1995
  - at 10 year: 76%
    - Sutherland DER, Transplantation, 2008

- **Pain relief in chronic pancreatitis:** 82%
The pancreas was cannulated for enzymatic infusion.

The pancreas was distended with enzymatic solution containing: 20 U/g pancreas GMP grade NB1 collagenase (Serva, USA) and 0.6 U/g pancreas neutral protease (Serva, USA).

Pancreas distension by using Perfusion Apparatus.
Islet cells processing

Islet digestion using **Ricordi®Islet Isolator** - automatic method

Islet collection for centrifugation
Islet cells infusion

Islets infused via an inferior mesenteric vein catheter into the portal system

4700 islet equivalent/kilogram (IEQ/kg)
Portal pressure was monitoring during infusion in ICU

Today - free of Insulin
Conclusions

- the **postoperative incidence of diabetes** is directly related to the extent of the **pancreatic resection**

- those patients who require only **distal pancreatectomy** or limited excavation of the pancreatic head develop diabetes far **less frequently** than those who require pancreaticoduodenectomy or near-total or total pancreatectomy