Octreotide and fibrin glue are overrated in the prevention of pancreatic fistula after pancreatic resection

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UCHSC Grand Rounds
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Complications of pancreaticoduodenectomy:

- Overall post-op morbidity: 50%
- Delayed gastric emptying: 30%
- Pancreatic fistula/leak: 8-25%
  - 20-25% of leaks led to mortality
- Abscess: 10%
  - 50% secondary to leak
- Exocrine insufficiency: 0-30%
- Mortality: <4%
What causes a pancreatic leak?

Theory: fistula effluent is pancreatic fluid, thus fistula must be caused by flow of pancreatic fluid.

Options:

1. **Decrease flow through** somatostatin
2. **Eliminate flow through** ductal obstruction
Theory: ↓ leak = ↓ morbidity & mortality

Somatostatin effects:
↓ Gastric emptying
↓ Gallbladder contraction
↓ Splanchnic blood flow
↓ Smooth muscle contractility
↓ VIP, glucagon, insulin
↓ Gastric acid secretion
↓ Pepsinogen
↓ Secretin
## Octreotide to prevent pancreatic leak:

<table>
<thead>
<tr>
<th>Study</th>
<th>#pts</th>
<th>CP/CA</th>
<th>Leak Octreotide Group</th>
<th>Leak Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeo, et al 2000</td>
<td>211</td>
<td>22/189</td>
<td>11%</td>
<td>9% (NS)</td>
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<tr>
<td>Hesse, et al 2005</td>
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No significant difference in mortality found in any of these studies.
What causes a pancreatic leak?

Theory: fistula effluent = pancreatic fluid, thus fistula must be caused by flow of fluid

1. Decrease flow through somatostatin
2. Eliminate flow through ductal obstruction
Hemostatic agents

Fibrin glue:

Gelfoam:

Surgicel:
Action of hemostatic agents:

- fibrinogen
  - → thrombin
  - → fibrin monomer
    - → fibrin polymer
      - → cross-linked insoluble fibrin polymer
        - (stable fibrin clot)
      - → Factor XIIIa
    - → Factor XIII
Fibrin glue occlusion of the pancreatic duct

Suc, et al, 2003  ductal occlusion  controls
182 pts  102  80
Pancreatic fistula  17%  15% (NS)

Ductal occlusion group had more:
- fibrotic pancreatic tissue
- reinforcement of anastomosis with fibrin glue
- octreotide prophylaxis

Fistula rate remained the same
Fibrin sealing of pancreatic anastomosis:

D’Andrea et al, 1994

**Post-operative fistula rate:**

<table>
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<tr>
<th>Fibrin seal</th>
<th>No seal</th>
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**Fistula rate remained the same**
What causes a pancreatic leak?

Risk factors for pancreatic leak after PD:

62 pts underwent PD for malignancy and pancreatitis
16% had a post-operative leak

Age
Gender
Jaundice
Nutritional status
Diagnosis
Prophylactic octreotide

No increased risk of pancreatic leak

Yang, et al 2005
## Risk factors for pancreatic leak after PD:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Leak Rate</th>
<th>p-value</th>
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<tbody>
<tr>
<td>duct ≥ 3mm</td>
<td>4.9%</td>
<td></td>
</tr>
<tr>
<td>duct &lt; 3mm</td>
<td>38%</td>
<td>0.002</td>
</tr>
<tr>
<td>Soft pancreas</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Hard pancreas</td>
<td>32%</td>
<td>0.004</td>
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*Yang, et al 2005*
Independent risk factors for leak:

Pancreatic texture

hard texture = good

soft texture = bad
Independent risk factors for leak: Pancreatic duct size

Big duct = good

Small duct = bad
Texture in the octreotide RCTs:

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No significant difference in mortality found in any of these studies.

Pancreatic texture may not make a difference.
Is there any evidence that flow of pancreatic fluid (presence, absence, character) causes post-operative leak?

NO.
Summary:

- **RCTs in past 5 years show no benefit to octreotide prophylaxis for pancreatic leak**
- **Ductal occlusion with fibrin glue does not decrease risk**
- **Anastomotic fibrin seal does not show convincing effect on leak rate**
Unanswered questions:

- Does pancreatic texture make a difference in leak rate?
- Does pancreatic fluid flow, volume or character cause pancreatic leaks?
- Can a product designed primarily to promote hemostasis do anything for pancreatic tissue synthesis?
Take home point:

“Surgical experience and technique appear to be the most important factors in determining the overall complications rates following elective pancreatic surgery”

Ridgeway & Stabile, 1996