The management of patients with pancreatic cancer: a difficult challenge and multidisciplinary approach

THE SURGEON POINT OF VIEW

GR Fronda

7th Division of Surgery
ASO San Giovanni Battista (Molinette), Turin.
Pancreatic cancer continues to pose an enormous challenge to clinicians and cancer scientists...

The cumulative risk (0-74 years) of developing a pancreatic cancer is 9.9% among males and 6.3% among females.

In Italy, incidence of pancreatic cancer is:
- 17 per 100,000 males
- 16.9 per 100,000 females

In United States, it is the 4th cause of cancer deaths:
- 37,000 diagnoses/year
- 33,000 deaths/year
SURVIVAL WITHOUT TREATMENT

Locally advanced disease: 6-10 months
Metastatic disease: 3-5 months

The surgical approach is the only potentially curative strategy.
The survival of patients who underwent pancreatetomy is **better** than that of patients without resection!

*American College of Surgeons of Chicago, National Cancer DataBase:*

<table>
<thead>
<tr>
<th>121,713 patients</th>
<th>STADIO IIA (T3N0) SURVIVAL 3 YEARS</th>
<th>STADIO IIA (T3N0) SURVIVAL 5 YEARS</th>
<th>STADIO IIB (T1-2-3N+) SURVIVAL 3 YEARS</th>
<th>STADIO IIB (T1-2-3N+) SURVIVAL 5 YEARS</th>
<th>STADIO III (T4anyN) SURVIVAL 3 YEARS</th>
<th>STADIO III (T4anyN) SURVIVAL 5 YEARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PANCREATECTOMY 18,743</td>
<td>23.8%</td>
<td>15.7%</td>
<td>14.4%</td>
<td>7.7%</td>
<td>11%</td>
<td>6.8%</td>
</tr>
<tr>
<td>NO RESECTION 102,970</td>
<td>4.1%</td>
<td>6.5%</td>
<td>3.8%</td>
<td>2%</td>
<td>3%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

But the late presentation and aggressive tumor biology of this disease means that only a minority (17%) of patients can undergo potentially curative surgery.
The most frequent localization of is the **head** (60%) and the optimal surgical procedure is PD (pancreaticoduodenectomy)

A very complex procedure:
- morbidity 40%
- mortality 3-5%

The margins of resection are crucial for the oncological results.

The margins of resection are:
- Anterior (bile duct)
- Pancreatic section
- Gastric (or duodenal) margin
- Posterior
The **posterior margin** is critical to obtain a radical resection: Retroperitoneal margin positivity is due to perineural or lymphatic invasion along the autonomic plexus surrounding the SMA and the celiac axis.

**R1 resection.**

**PANCREATIC CANCER**

**What’s a R1 resection?**
but the aims of surgery are to achieve

**R0 resection**: complete clearance of macroscopic tumour with clear microscopic resection margins, even if there are lymph node metastases

and above all to avoid

**R2 resection**: grossly incomplete resection, with macroscopical residual disease

At least 35% of patients are *histologically* staged as

**R1 resection**: complete clearance of macroscopic tumour with positive resection margins (retroperitoneal margin)
The R classification is related to the survival:
R1 is related to tumors with a more aggressive biological behaviour and is a negative prognostic factor.

The median survival for R1 patients is worse than R0:
9-10 months *versus* 16.9 months,
Only in the R0 resection
the actuarial survival to 5 years is 15-25%!

The goals of surgeon in presence of a pancreatic lesion are:

- To obtain a *correct diagnosis and a proper surgical indication, with an optimal DIFFERENTIAL DIAGNOSIS*
- To select the *patients with unresectable tumor from the patients with resectable lesion* to avoid useless and dangerous laparotomy with an optimal *PREOPERATIVE STAGING*
• DIFFERENTIAL DIAGNOSIS
• PREOPERATIVE STAGING
PANCREATIC CANCER - DIFFERENTIAL DIAGNOSIS

PANCREATIC LESIONS

Solid mass
- ductal adenocarcinoma
- chronic pancreatitis
- other types (lymphoma, neuroendocrine tumors, mesenchymal tumors)

Cystic lesion
- ductal mucinous adenocarcinoma (colloid carcinoma)
- mucinous cystic tumors
- serous tumors

Dilatated main pancreatic duct
- chronic pancreatitis
- ductal adenocarcinoma
- intraductal papillary mucinous tumor (IPMT)
PANCREATIC CANCER-DIFFERENTIAL DIAGNOSIS

PANCREATIC LESIONS

**Solid mass**
- ductal adenocarcinoma
- chronic pancreatitis
- other types (lymphoma, neuroendocrine tumors, mesenchymal tumors)

**Cystic lesion**
- ductal mucinous adenocarcinoma (colloid carcinoma)
- mucinous cystic tumors
- serous tumors

**Dilatated main pancreatic duct**
- chronic pancreatitis
- ductal adenocarcinoma
- intraductal papillary mucinous tumor (IPMT)
SOLID MASS

It’s very difficult to distinguishing among adenocarcinoma and chronic pancreatitis

- Groove pancreatitis (duodenal cystic distrophy)
- Mass forming (autoimmune with response to steroidal therapy)

the CT-scan is not satisfactory!

EUS, EUS-FNA
SOLID MASS

Echoendoscopic features suggestive for malignancy
- absence echodoppler signal
- etereogenous mass

EUS-FNA

- lower risk of neoplastic seeding than CT-FNA
- possibility of lymph-nodal biopsy

### EUS-FNA

<table>
<thead>
<tr>
<th></th>
<th>Sensibility</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS</td>
<td>63.6%</td>
<td>75%</td>
<td>33.3%</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>72.7%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EUS-FNA Biopsy</th>
<th>Specificity</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph-nodal</td>
<td>100%</td>
<td>67%</td>
</tr>
<tr>
<td>Mass</td>
<td>80%</td>
<td>86%</td>
</tr>
</tbody>
</table>
negative biopsy
elevated clinical suspicious resectable tumor

SURGERY is indicated!
## PANCREATIC CANCER-DIFFERENTIAL DIAGNOSIS

### PANCREATIC LESIONS

#### Solid mass
- ductal adenocarcinoma
- chronic pancreatitis
- other types (lymphoma, neuroendocrine tumors, mesenchymal tumors)

#### Cystic lesion
- ductal mucinous adenocarcinoma (colloid carcinoma)
- mucinous cystic tumors
- serous tumors

#### Dilatated main pancreatic duct
- chronic pancreatitis
- ductal adenocarcinoma
- intraductal papillary mucinous tumor (IPMT)
CYSTIC LESION

Echoendoscopic features of malignancy:

- unilocular
- macrocystic inclusions >20 mm or vegetations
- focal wall thickening (mural nodules)
- calcified spots
- thickened septations
- sediment or mucous

Cyst fluid analysis:
- CEA and CA 19-9
- Mucin

Sensibility: 100%
Specificity: 78%
PPV: 94%
NPV: 100%

O’Toole Gastrointest Endosc 2004; 59 (7): 823-29.
CYSTIC LESION

SEROUS CYSTOADENOMA

- **microcystic**: (fine wall, alvear septations)
  - benigns, not surgery!
  - CT-scan is adequate

- **macrocystic**: is difficult to distinguishing from mucinous cystoadenoma
  - EUS, EUS-FNA
  - useful in the lesions < 2 cm
# Pancreatic Lesions

## Pancreatic Cancer-Differential Diagnosis

### Pancreatic Lesions

<table>
<thead>
<tr>
<th>Type</th>
<th>Conditions</th>
</tr>
</thead>
</table>
| **Solid mass**                            | • ductal adenocarcinoma
• chronic pancreatitis
• other types (lymphoma, neuroendocrine tumors, mesenchymal tumors) |
| **Cystic lesion**                         | • ductal mucinous adenocarcinoma (colloid carcinoma)
• mucinous cystic tumors
• serous tumors                             |
| **Dilatated main pancreatic duct**       | • chronic pancreatitis
• ductal adenocarcinoma
• intraductal papillary mucinous tumor (IPMT) |
DILATATED PANCREATIC DUCT

INTRADUCTAL PAPILLARY-MUCINOUS TUMORS (IPMT)

Mucinous producing neoplasms with dilatation of main pancreatic duct and/or collaterals

Can evolve in carcinoma!

The risk is among 29-62%
The risk of lymph nodal metastases is 5-31%

INTRADUCTAL PAPILLARY-MUCINOUS TUMORS (IPMT)

EUS: necessary for lesions <2 cm

Sensibility 86%
Specificity 99%

RESECTIVE SURGERY

- Ductal adenocarcinoma
- Chronic pancreatitis - groove focal symptomatic
- Mucin producing tumors (cystic and IPMT)
- Neuroendocrine tumors

DERIVATIVE SURGERY

- Chronic pancreatitis or pseudocyst
NO SURGERY

- Asymptomatic serous tumors
- Mass forming autoimmune pancreatitis
- Lymphoma
• DIFFERENTIAL DIAGNOSIS
• PREOPERATIVE STAGING
PANCREATIC CANCER-PREOPERATIVE STAGING

RESECTABILITY
(CRITERIA ANDERSON CANCER CENTER)

**RESECTABLE**
Absence of tumor extension to the SMA, celiac axis, CHA and a patent SM-PV confluence (en bloc resection of the SMV and/or PV if necessary).

**UNRESECTABLE**
Locally advanced tumor that encases the adjacent arteries (celiac axis, SMA, or both) or that occlude the SMV, PV or SMPV confluence (*encasement*: a low-density tumor involves >180° circumference of the vessel)

BORDERLINE

Tumors exhibiting

- encasement of a short segment of the epatic artery, without evidence of the tumor extension to the celiac axis,
- abutment of the SMA involving <180° of the circumference of the artery;
- or short-segment occlusion of the SMV, PV or SMPV confluence with a suitable option of vascular reconstruction

BORDERLINE – RESECTABLE TUMORS

EUS
# ROLE OF EUS

<table>
<thead>
<tr>
<th>Hunt, 2002</th>
<th>sensibility</th>
<th>stadiation T</th>
<th>stadiation N</th>
<th>vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>69-85%</td>
<td>30-45%</td>
<td>50-55%</td>
<td>62-75%</td>
</tr>
<tr>
<td>EUS n</td>
<td>94-100%</td>
<td>82%</td>
<td>64-72%</td>
<td>92-95%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Queneau, 2001</th>
<th>sensibility</th>
<th>specificity</th>
<th>positive predictive value</th>
<th>negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS n</td>
<td>89%</td>
<td>100%</td>
<td>100%</td>
<td>91.7%</td>
</tr>
</tbody>
</table>

assess vascular invasion in borderline tumors at CT-scan

- peripancreatic collateral circles
- absence of vascular interface
- tumoral tissue along the major pancreatic vessels

Detection of “true” resectable lesions
The intraoperative biopsy have a lower sensibility
UNRESECTABLE TUMOR

Not palliative intervention, eventually gastrojejunostomy, in young patients, to prevent late gastric obstruction
1994-2007

Patients observed: 331

CT scan: 331 (100%)

EUS: 85 (26%)

Pancreatic resections: 248 (75%)
PANCREATIC CANCER- THE ROLE OF EUS

CONCLUSIONS

- Detection of lesion (in suspicious)
- Differential diagnosis between benign and malignant lesions
- Sampling of lesions and lymph nodes minimizing the risk of seeding
- Assess the local extent and vascular invasion of the tumor (staging and resectability)
- Biopsy the lesion for cytopathological confirmation if the tumor is unresectable
CT-scan and the EUS are essential tools for the surgeons

- to achieve \textit{R0} resection
- to avoid useless laparotomy!