Cancro del pancreas

Caso Clinico

M, 36 aa va dal proprio Medico curante per fastidio / lieve dolore addominale e per una sensazione di malessere generale

Viene posta diagnosi di “Probabile IBS / GERD” e per questo motivo il paziente viene trattato con PPI (omeprazolo, 20mg / die)

Caso Clinico

Nonostante la terapia i sintomi persistono; poco tempo dopo (circa 3-4 mesi), il paziente sviluppa ittero con spiccate alterazioni dei test di funzionalità epatica (aumento gGT, Fosf Alc, AST, ALT, etc)

ECO addome: VBP dilatata (>8mm)

ERCP: stent biliare per correggere una stenosi poco sopra la papilla di Vater – patologia biliare ? Coledocica ? Colecistica ?

Caso Clinico

A distanza di 1 aa dall'inizio della sintomatologia, il paziente viene ricoverato per la comparsa di dolore addominale diffuso particolarmente severo (VAS: 10)

ECO: massa pancreatica localizzata alla testa del pancreas;

TAC: massa della regione cefalica del pancreas di 4.5 x 2.5 cm; dilatazione della VBP (>1 cm) + vie biliari intraepatiche ed intrapancreatiche

ECO-endoscopia (EUS) + FNA della testa del pancreas

Caso Clinico

Diagnosi: adenocarcinoma della testa del pancreas;

Staging mediante TAC total body: nessuna evidenza di diffusione locale né metastasi (organi, linfonodi)

Il paziente viene visto dal Collega Chirurgo per considerare un'intervento di cefalo-duodeno pancreasectomia (Whipple's procedure)

Patologie neoplastiche pancreatiche

● Exocrine = 95%

● Endocrine = 5%

Entità nosografica	%	
Adenocarcinoma duttale	80	
varianti del duttale	5	●
Cistoadenoma sieroso	1	●
Neoplasia mucinosa cistica (cistoadenoma mucinoso)	1	●
Neoplasia intraduttale papillare mucinosa	5	●
Carcinoma a cellule acinari	1	●
Pancreatoblastoma	1	●
Neoplasia solida-pseudopapillare	1	●
Neoplasie neuroendocrine	5	●

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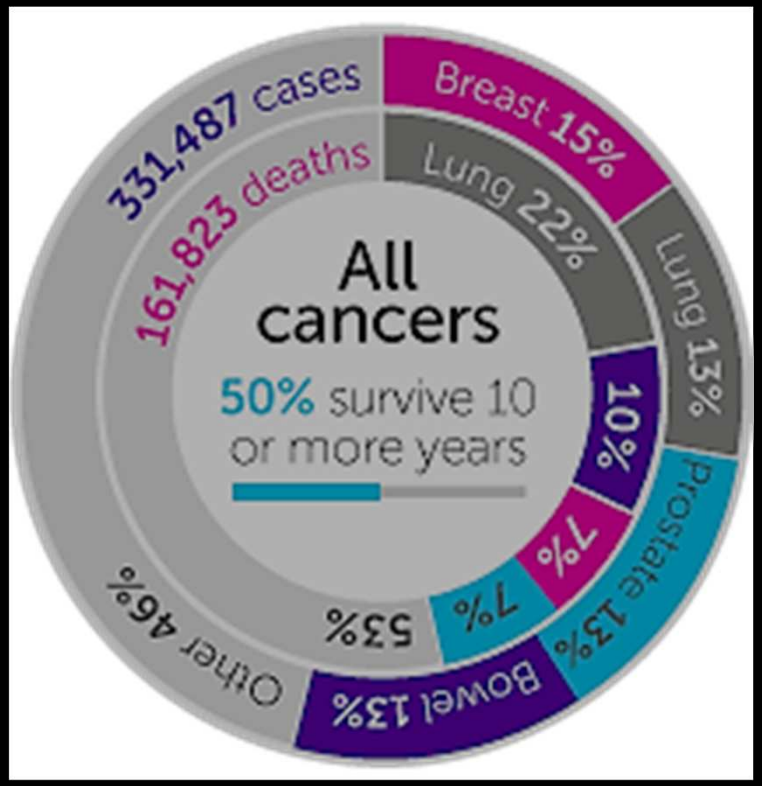
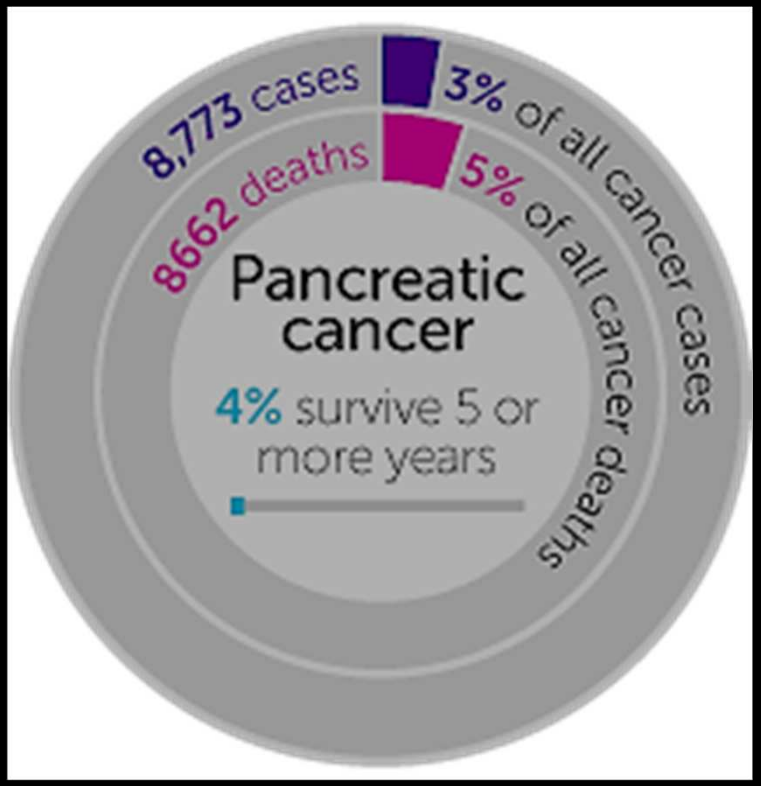
…only 2% are benign !!!

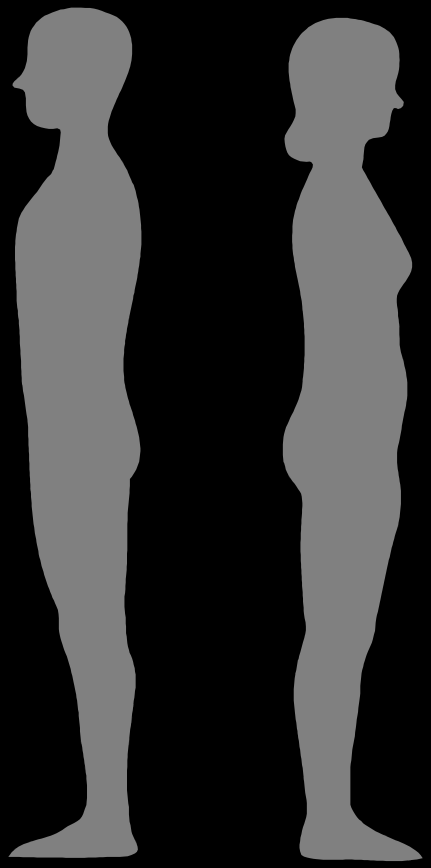
Impact of pancreatic cancer





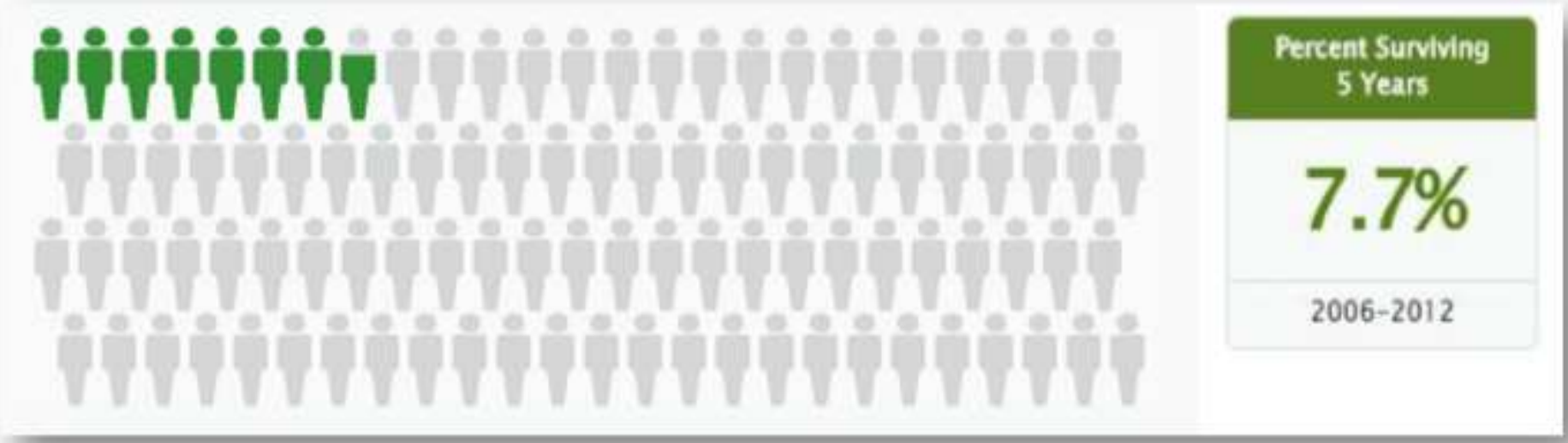
Estimated Cancer Cases (US - in 2007)

Men 766,860			Women 678,060	
Prostate	29%		26%	Breast
Lung & bronchus	15%		15%	Lung & bronchus
Colon & rectum	10%		11%	Colon & rectum
Urinary bladder	7%		6%	Uterine corpus
Non-Hodgkin lymphoma	4%		4%	Non-Hodgkin lymphoma
Melanoma of skin	4%		4%	Melanoma of skin
Kidney	4%		4%	Thyroid
Leukemia	3%		3%	Ovary
Oral cavity	3%		3%	Kidney
Pancreas	2%		3%	Leukemia
All Other Sites	19%		21%	All Other Sites



Pancreatic cancer

Pancreatic cancer (PC) is the fourth leading cause of cancer death in Western societies. However, it is projected to be the second within a decade[1-2].



Due to the aggressive nature of PC, its late presentation and the lack of effective screening, around 50% of patients are metastatic at the time of diagnosis.
5-yrs survival in mPC is around 1%[3].

1. Rahib L. *et al*, *Cancer Res*, 2014
2. SEER database, last update July 2016
3. Kleef J *et al*, *Nat Rev Dis Primers*, 2016

Patologie neoplastiche pancreatiche

Entità nosografica	%
Adenocarcinoma duttale	80
varianti del duttale	5
Cistoadenoma sieroso	1
Neoplasia mucinosa cistica (cistoadenoma mucinoso)	1
Neoplasia intraduttale papillare mucinosa	5
Carcinoma a cellule acinari	1
Pancreatoblastoma	1
Neoplasia solida-pseudopapillare	1
Neoplasie neuroendocrine	5

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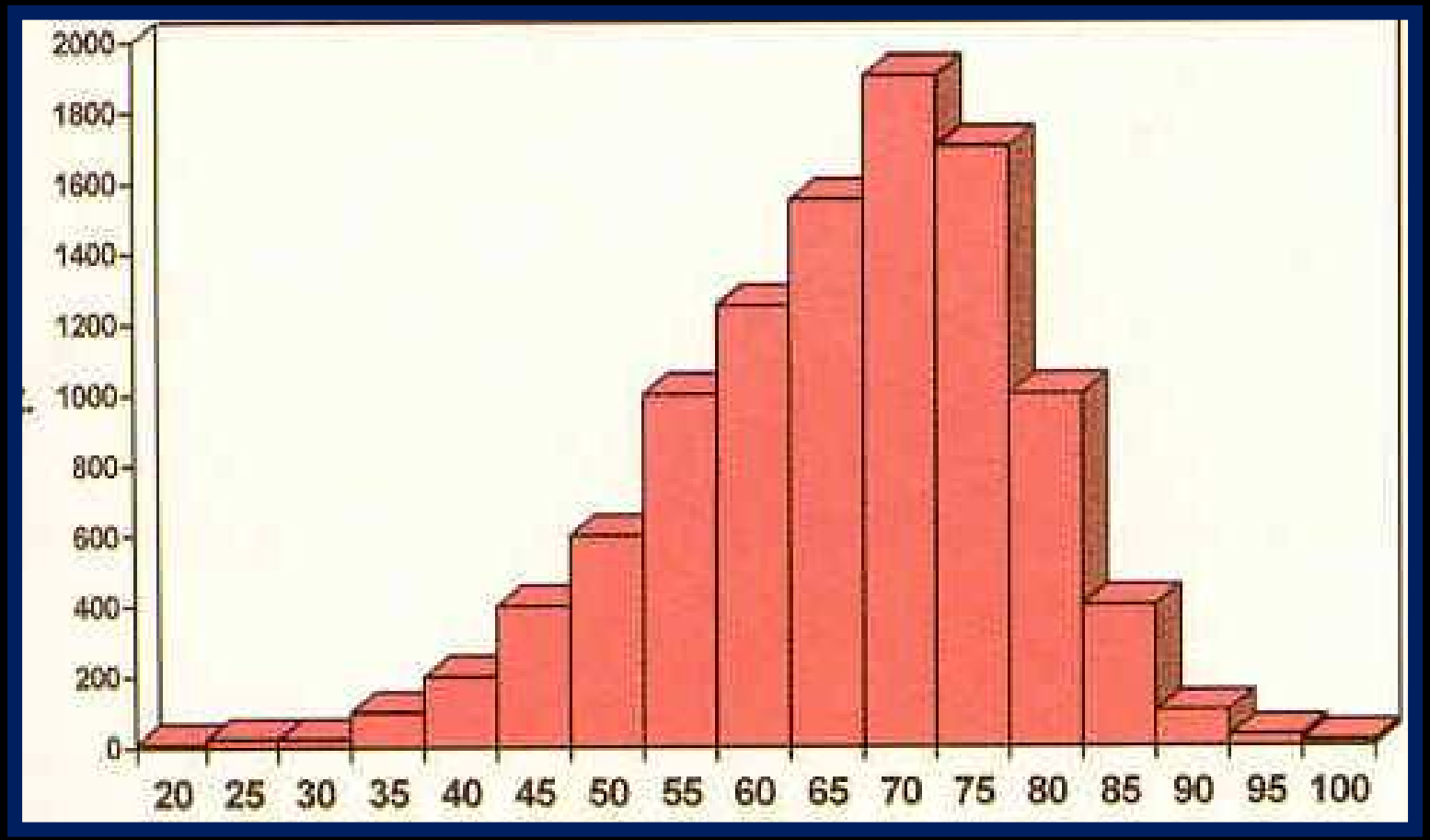
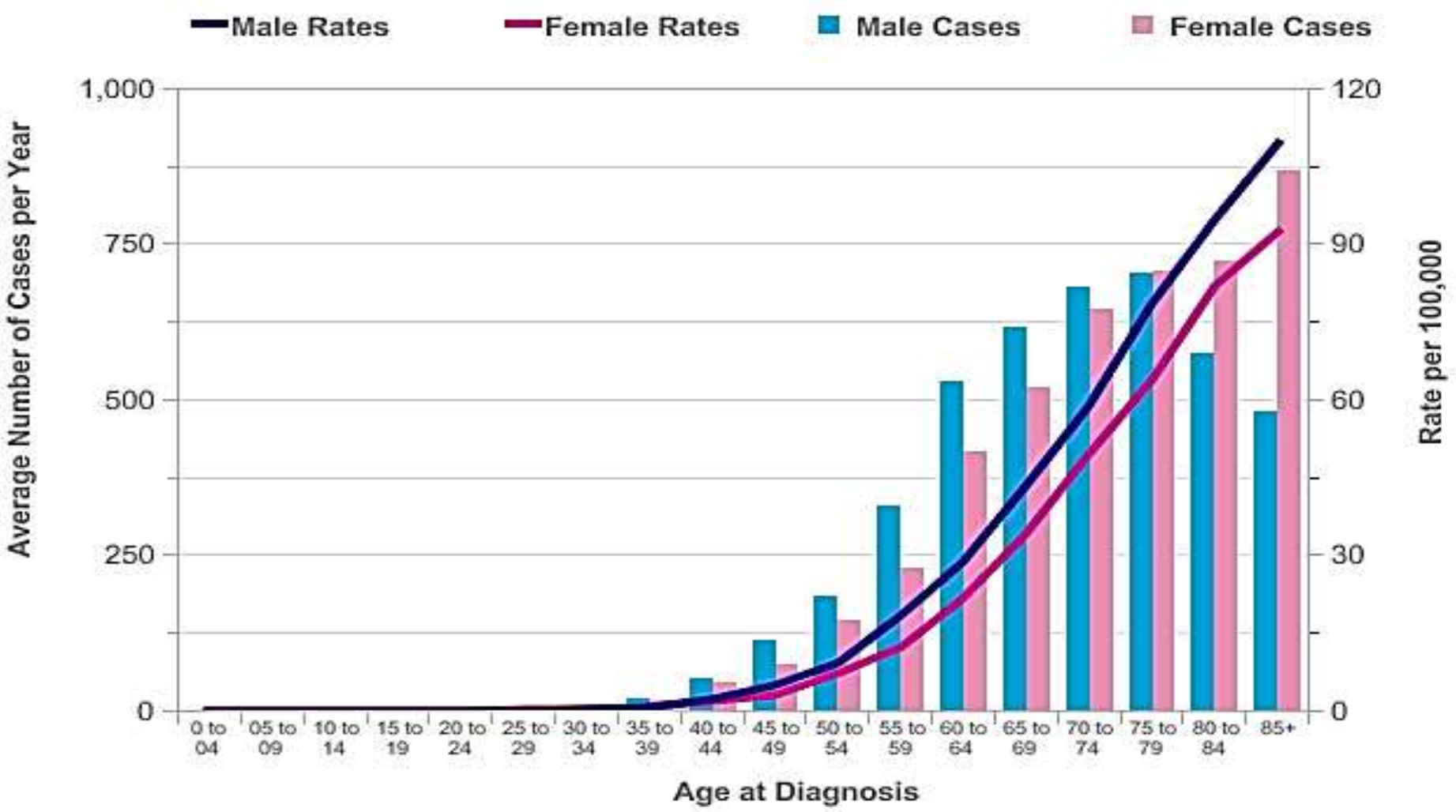
ADENOCARCINOMA DUTTALE

Sesso: **UOMINI (maschi/femmine= 2/1)**



Incidence


Male Rates
Female Rates
Male Cases
Female Cases
Average Number of Cases per Year
1,000
750
500
250
0
120
90
60
30
0
Rate per 100,000
0 to 04
05 to 09
10 to 14
15 to 19
20 to 24
25 to 29
30 to 34
35 to 39
40 to 44
45 to 49
50 to 54
55 to 59
60 to 64
65 to 69
70 to 74
75 to 79
80 to 84
85+
Age at Diagnosis

Risk Factors

Smoking
Genetic factors
Chronic Pancreatitis
Hereditary Pancreatitis
Age >70
Type II DM
Obesity
High fat diet
Previous gastric surgery
Sclerosing Cholangitis
Helicobacter Pylori

Hereditary cancer syndromes

- **Peutz-Jeghers** (autosomal dominant; hamartomatous polyps in the GI tract + hyperpigmented macules ['melanosis'] on lips and oral mucosa; incidence: 1 in 25.000-300.000 births)
- **FAMMM** (Familial Atypical Multiple Mole Melanoma Syndrome: autosomal dominant; multiple melanocytic nevi [>50]; family history of melanoma; *CDKN2A* mutations)
- **Familial breast/ovarian cancer** (5–10% of heritable breast cancers; 3–13% of ovarian cancers)
- **FAP / HNPCC**
- **Hereditary Pancreatitis**
- **Von Hippel-Lindau** (hemangioblastomas + fluid cysts)
- **Cystic Fibrosis**

Symptoms of Pancreatic Cancer

If you persistently experience one or more of these symptoms which are not normal for you, **DO NOT IGNORE THEM!**

Contact your GP straight away. Or call the NHS 111 Service.

- Low mood or depression
- Upper abdominal pain
- Pain on eating
- Jaundice (yellowing of the skin and eyes)
- Pale and smelly stools that don't flush easily
- Unexplained weight loss
- Upper back pain
- Indigestion not responding to prescribed medication
- New onset diabetes not associated with weight gain
- Fatigue

Common Misdiagnoses

Gallstones
Irritable Bowel Syndrome
Indigestion
Gastritis
Gastroenteritis
Liver disease

Pancreatic Cancer Action

Chiltlee Manor, Haslemere Road, Liphook, Hampshire GU30 7AZ
Registered Charity: 1137689 | www.pancreaticcanceraction.org | 0303 040 1770

Clinical features

Symptoms and signs vary depending on the anatomic location of the tumor (head vs. body / tail):

- **Head of the pancreas**
  - Obstruction of the bile duct: jaundice 30%; pruritus; painless in about 10%; most will have some pain, but not biliary colic.
  - Obstruction of the small intestine or stomach: nausea, vomiting; weight loss (80%).
- **Body / tail of the pancreas**:
  - Upper abdominal / back pain (70-80%): may be continuos / intermittent, worse with eating, and usually associated with a poor prognosis;
  - Weight loss;
  - Fatigue

Other symptoms

- New onset type 2 DM (20%)
  - Normal weight or, more commonly, underweight patients
- Resistant dyspepsia / persistent epigastric pain
- IBS like symptoms in those >45 years
  - very rare as a new onset symptom at this age
- Altered bowel habit
  - Increased bowel movement frequency and steathorrea (10%)
- Venous thromboembolism (Trousseau's sign or *tromboflebitis migrans*)
  - Heralding an underlying abdominal malignancy
- Mood disorders

Laboratory tests

- Full blood count
  - anaemia rare except for ampullary tumours (bleeding)
- Liver function tests
  - Obstructive jaundice
  - Elevated gGT / Alk Phos may precede ↑bilirubin
- Serum glucose
  - Diabetes (20%) or impaired glucose tolerance (20%)
- CA19-9
  - Sensitivity of ~80% and a specificity of 83%
  - Normal levels do not exclude diagnosis
  - Better for treatment monitoring

Semeiotica strumentale

I livello

Ecografia senza e con mdc

TC multidetettore toraco addominale

Diagnosi di massa pancreatica sospetta

Stadiazione clinica cTNM

Criteri di resecabilità

Table 1

American Joint Committee on Cancer (AJCC) TNM Staging of Pancreatic Cancer (2010)

Because only a few patients with pancreatic cancer undergo surgical resection of the pancreas (and adjacent lymph nodes), a single TNM classification must apply to both clinical and pathologic staging.

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ*
T1	Tumor limited to the pancreas, 2 cm or less in greatest dimension
T2	Tumor limited to the pancreas, more than 2 cm in greatest dimension
T3	Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
T4	Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)

* This also includes the "PanInIII" classification.

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant Metastases (M)

M0	No distant metastases
M1	Distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science+Business Media, LLC (SBM). (For complete information and data supporting the staging tables, visit www.springer.com.) Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse or further distribution without the expressed, written permission of Springer SBM, on behalf of the AJCC.

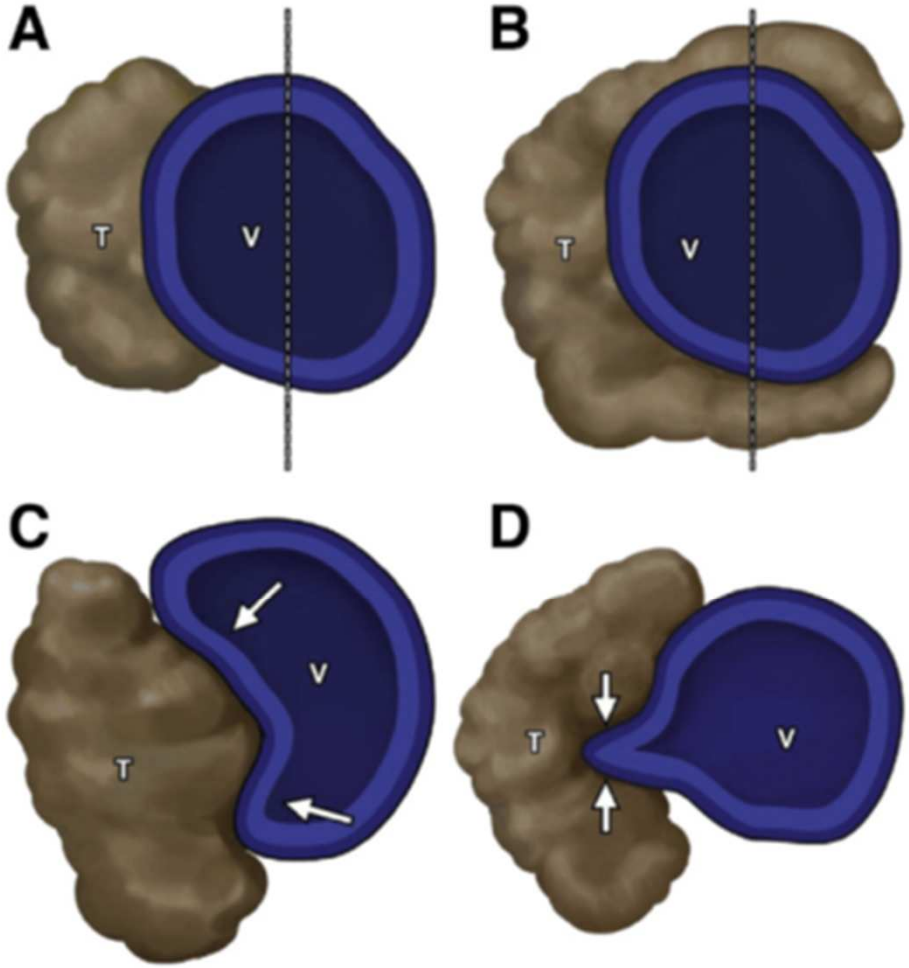


Figure 3. Venous tumor contact. (***A***) Less than or equal to 180° tumor contact without deformity. (***B***) More than 180° tumor contact without deformity. (***C***) Less than or equal to 180° tumor contact with deformity (arrows). (***D***) Tear drop deformity (arrows). *T* = tumor, *V* = vein. Dashed line = 180° of lumen circumference.

hepatic arteries,

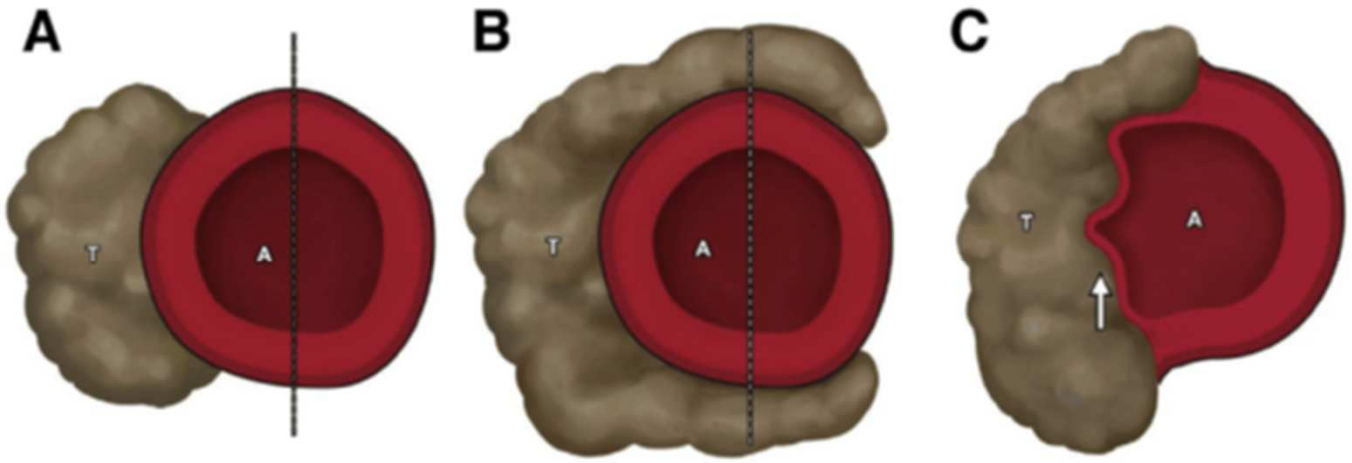


Figure 2. Arterial tumor contact. ***(A)*** Less than or equal to 180° tumor contact without deformity. ***(B)*** More than 180° tumor contact without deformity. ***(C)*** Tumor contact with deformity (arrow). *A* = artery, *T* = tumor. Dashed line = 180° of lumen circumference.

Semeiotica strumentale

II-III livello

RM complementare alla TC multidetettore

EUS in casi selezionati: 1) quando la neoplasia è molto piccola;
2) per eseguire una FNA o FNB

PET/TC 18F-FDG valutazione metastasi a distanza in casi selezionati (più utile nel follow-up dei resecati)

Treatment strategies

- Resectable vs. Locally-Advanced vs. Metastatic disease
- Adjuvant vs. Neoadjuvant treatment
- Surgery vs. Chemotherapy vs. Radiation therapy

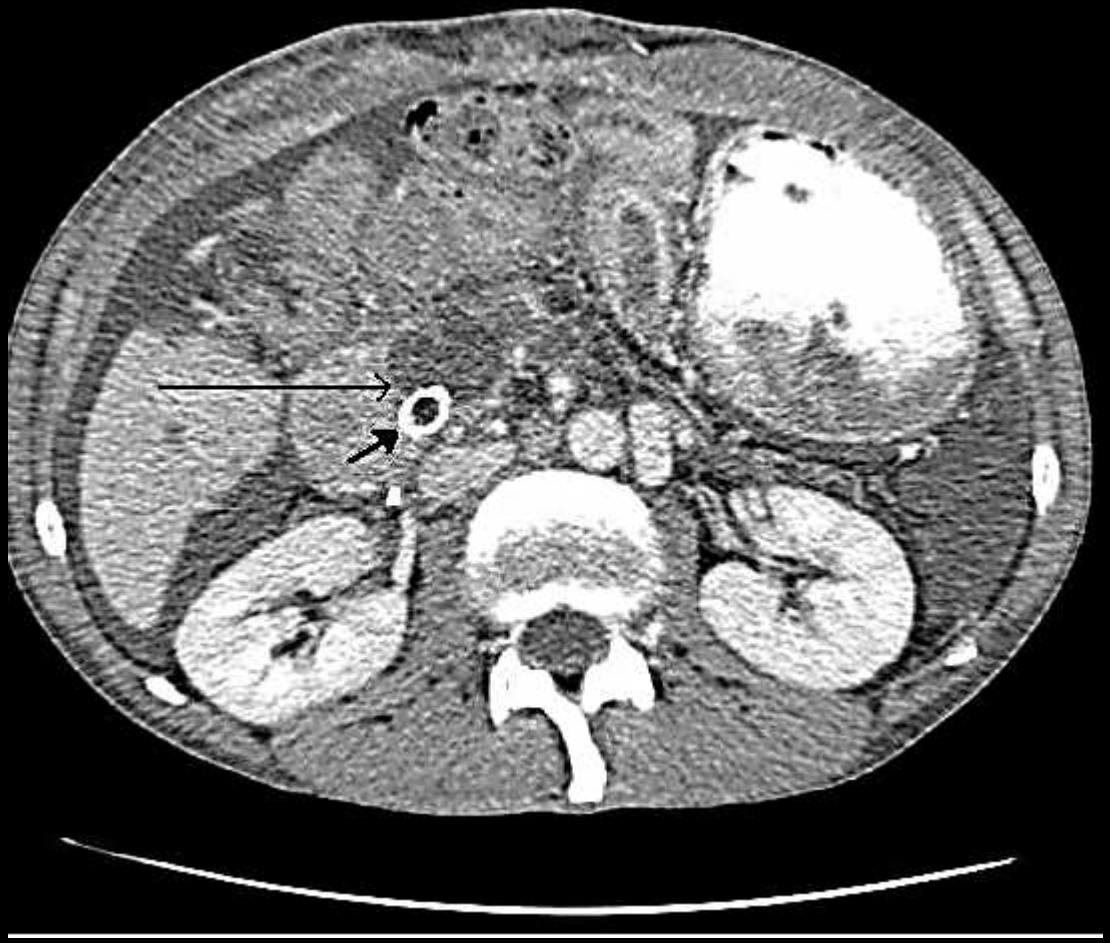
Surgery

- Surgical resection: only potentially curable treatment option
- However, 5-yr survival rate is only about 25-30% for node-negative disease and <10% for non-metastatic disease
- Due to the late presentation, only 15-20% of cases are resectable at the time of diagnosis…

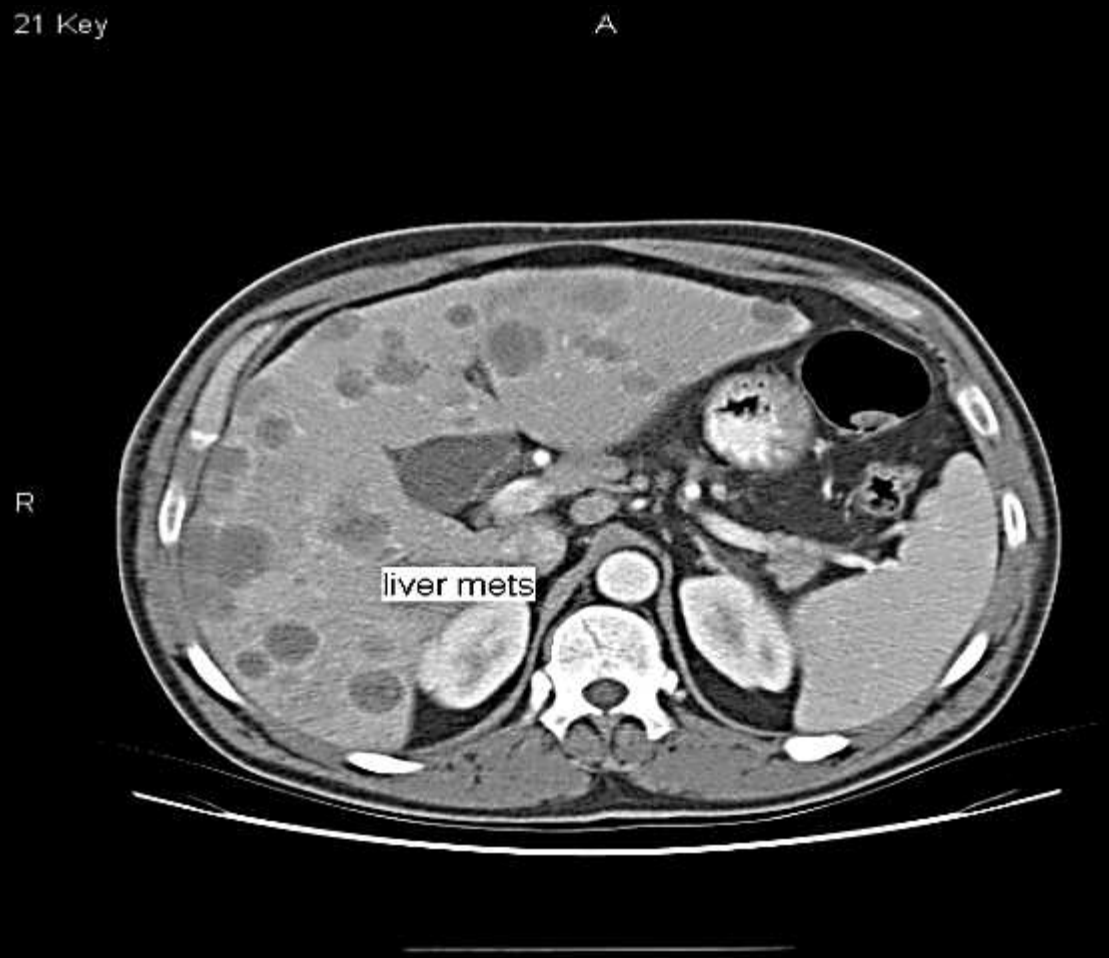
Resectability: When is it possible ?

- Absolute contraindications include: metastasis to the liver, peritoneum, omentum, or any extrabdominal site
- Most surgeons require that the tumor does not involve sites that would not be encompassed within the resection, and does not involve the adjacent critical structures such as SMA / SMV, portal vein, celiac axis, or hepatic artery

Resectable



Unresectable



Chemotherapy

- >80% now receive adjuvant chemotherapy after surgery (Gemcitabine +/- others)

- Minority of unresectable patients fit for palliative chemotherapy (Folfirinox)
  - 50% if locally advanced
  - 36% if metastatic

- Role of neo-adjuvant chemotherapy currently being explored
  - ESPAC-5

Palliation of symptoms

- Jaundice – biliary stent
- Duodenal obstruction – duodenal stent vs. bypass procedure
- Delayed gastric emptying – prokinetic agents may be helpful
- Pain – celiac plexus block, narcotics, palliative radiation
- Depression – antidepressants and emotional support
- Malabsorption / Cachexia – consider pancreatic enzyme replacement
- Ascites – palliative paracentesis, gentle diruesis

Patologie neoplastiche pancreatiche

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Pancreatoblastoma	1
Neoplasia solida-pseudopapillare	1
Neoplasie neuroendocrine	5

AIOM 2015

NEOPLASTICHE

Neoplastic cysts (60%)
- Ductal lineage
  - Mucinous type (30%)
    - Intraductal papillary mucinous neoplasm
    - Mucinous cystic neoplasm
    - Intraductal oncocytic papillary neoplasm
    - "Retention cyst," "mucocele," and "mucinous nonneoplastic cyst"
    - Cystic change in ordinary ductal adenocarcinoma and other invasive carcinomas
  - Serous (clear-cell) type (20%)
    - Serous cystadenoma
    - Oligocystic (macrocystic) variant of serous cystadenoma
    - von Hippel-Lindau syndrome–associated pancreatic cysts
    - Serous cystadenocarcinoma
  - Not otherwise specified
    - Intraductal tubular carcinoma
- Endocrine lineage (<5%)
  - Cystic pancreatic endocrine neoplasm
- Acinar lineage (<1%)
  - Acinar cell cystadenoma (cystic acinar transformation)
  - Acinar cell cystadenocarcinoma
  - Cystic/Intraductal acinar cell carcinoma
- Endothelial lineage (<1%)
  - Lymphangioma
- Mesenchymal lineage (<1%)
- Undetermined lineage (5%)
  - Solid-pseudopapillary neoplasm
- Other
  - Mature cystic teratoma

NON NEOPLASTICHE

Injury-related and inflammation-related cysts (30%)
- Pseudocyst
- Paraduodenal wall cyst
- Infection-related cysts

Congenital cysts (<1%)
- Duplication (enterogenous) cysts
- Duodenal diverticula
- Others

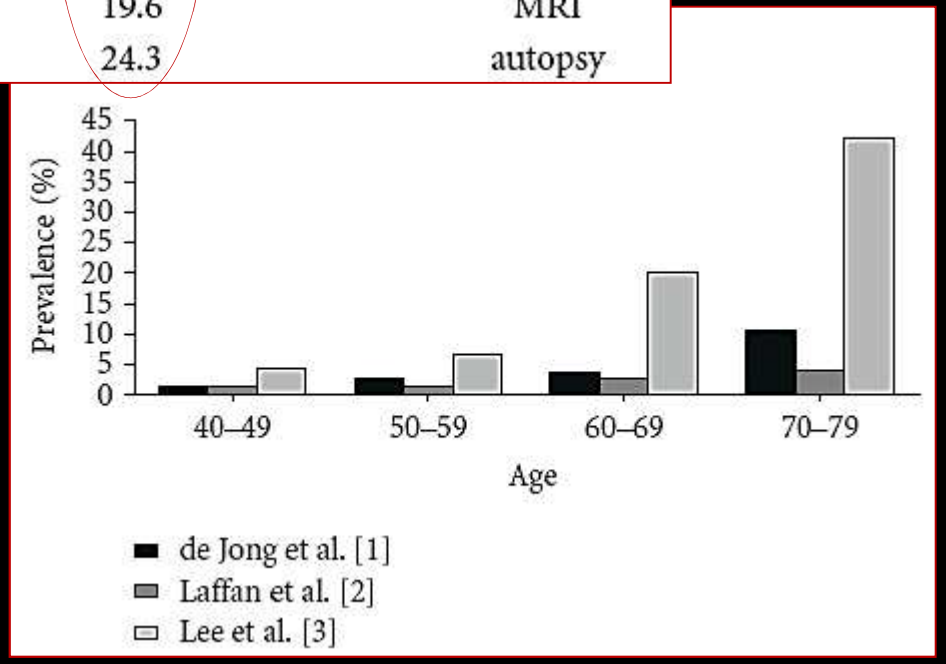
Miscellaneous cysts (<5%)
- Lymphoepithelial cyst
- Squamoid cyst of pancreatic ducts
- Epidermoid cysts within intrapancreatic accessory spleen
- Cystic hamartoma
- Endometriotic cysts
- Secondary tumors

Basturk O et al
Arch Pathol Lab Med 2009

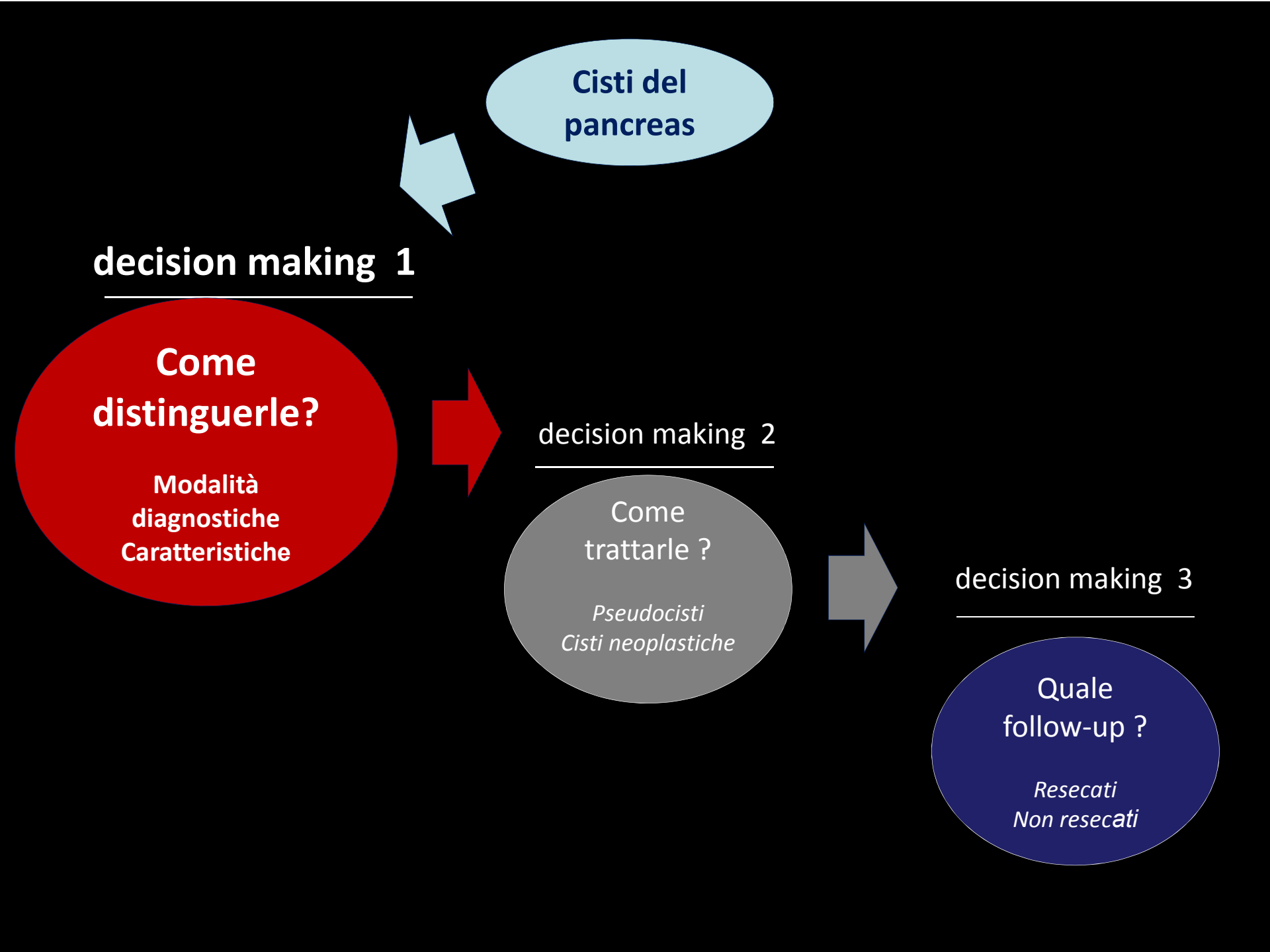
TUMORI CISTICI DEL PANCREAS

Patologia in crescita….45-70% lesioni cistiche incidentali…

Study	Number of patients	Prevalence (%)	Technique
de Jong et al. [1], 2010	2803	2.4	MRI
Laffan et al. [2], 2008	2832	2.6	CT
Lee et al. [3], 2010	616	13.5	MRI
Spinelli et al. [4], 2004	24039	1.2	MRI and CT
Zhang et al. [5], 2002	1444	19.6	MRI
Kimura et al. [6], 1995	300	24.3	autopsy



De Jong K et al.
Gastroenterology Research & Practice 2012


Cisti del pancreas
decision making 1
Come distinguerle?
Modalità diagnostiche
Caratteristiche
decision making 2
Come trattarle ?
Pseudocisti
Cisti neoplastiche
decision making 3
Quale follow-up ?
Resecati
Non resecati

Le metodiche di imaging

1 TC spirale multislice addome; CWRM (con secretina) (evidence level 2-3)

diagnosi	accuratezza diagnostica
Pseudocisti Vs Cisti neoplastica	73.5%
Mucinoso Vs Non mucinoso	82-85%
Benigno Vs Maligno	85%

Chalian H, et al JOP 2011;
Khalid A, et al Am J Gastroenterology 2007;
Sahani DV, AJR 2011;
Kwon RS Curr Opin Gastroenterol 2012.

2 EUS-FNA (evidence level 2)

Table 4. Accuracy of the 3 Primary Tests for Differentiating Between Mucinous and Nonmucinous Cystic Lesions

	EUS morphology	Cytology	CEA
Sensitivity	32/57 (56.1%)	19/55 (34.5%)	42/56 (75%)
Specificity	25/55 (45.4%)	45/54 (83.3%)	46/55 (83.6%)
Accuracy	57/112 (50.9%)	64/109 (58.7%)[a]	88/111 (79.2%)[b,c]

Table 5. Accuracy of Combination of Tests for Diagnosing Mucinous Cystic Lesions of the Pancreas

	EUS morphology or cytology	EUS morphology or cytology or CEA	Cytology or CEA
Sensitivity[a]	70	91	82
Specificity	38	31	71
Accuracy	54	62	77[b]

Brugge et al Gastroenterology 2004

CEA>192ng/mL

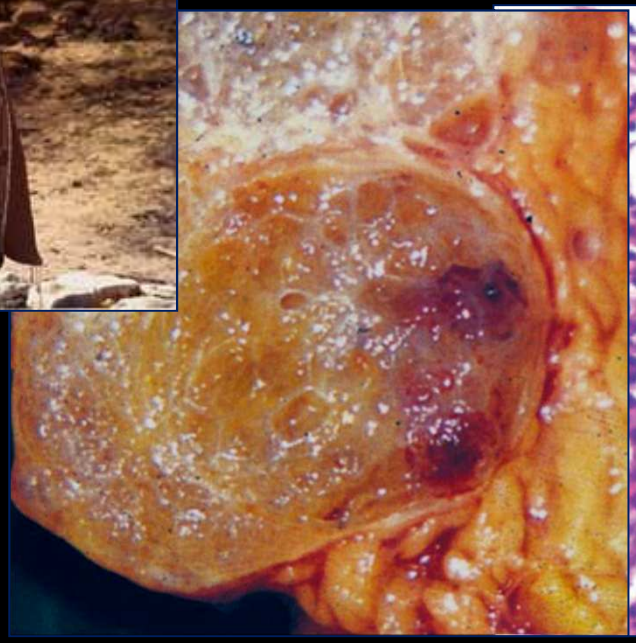
TUMORE CISTICO SIEROSO (TCS)

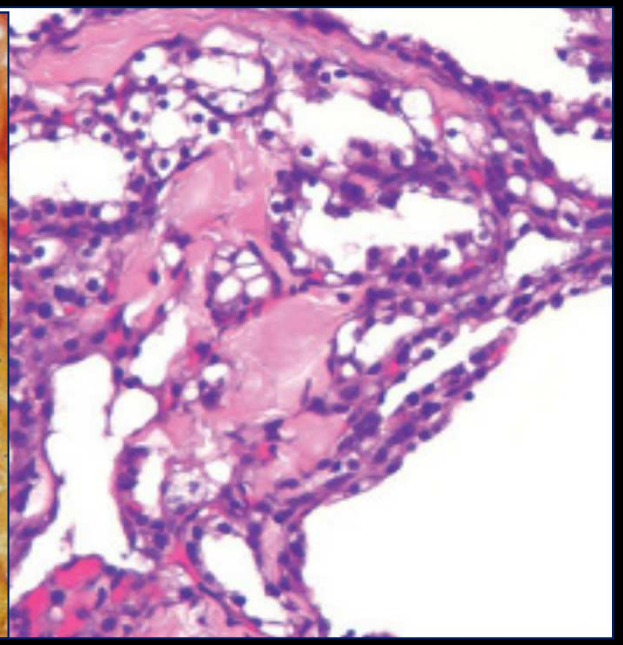
TUMORE CISTICO MUCINOSO (TCM)

NEOPLASIA PAPILLARE INTRADUTTALE MUCINOSA (IPMN)

TUMORE CISTICO SIEROSO

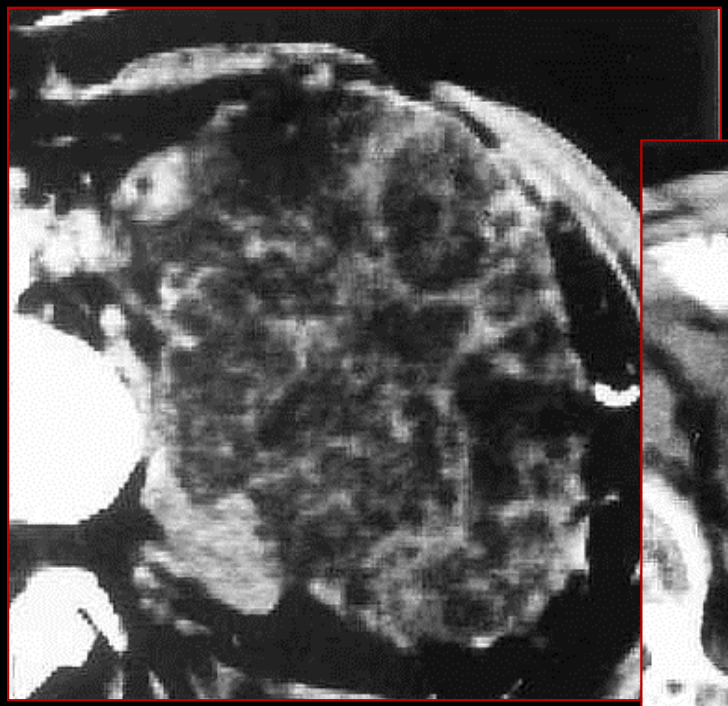
Origina da cellule centro-acinari
e/o del sistema duttale

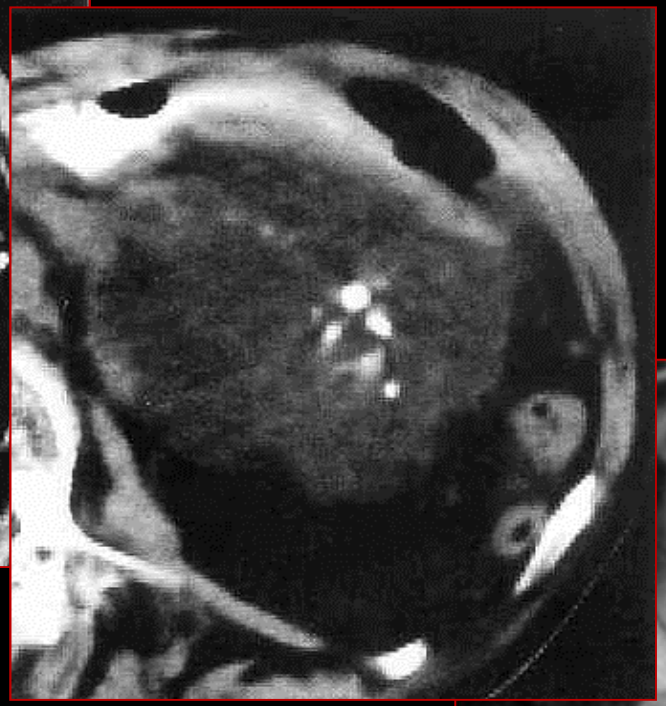




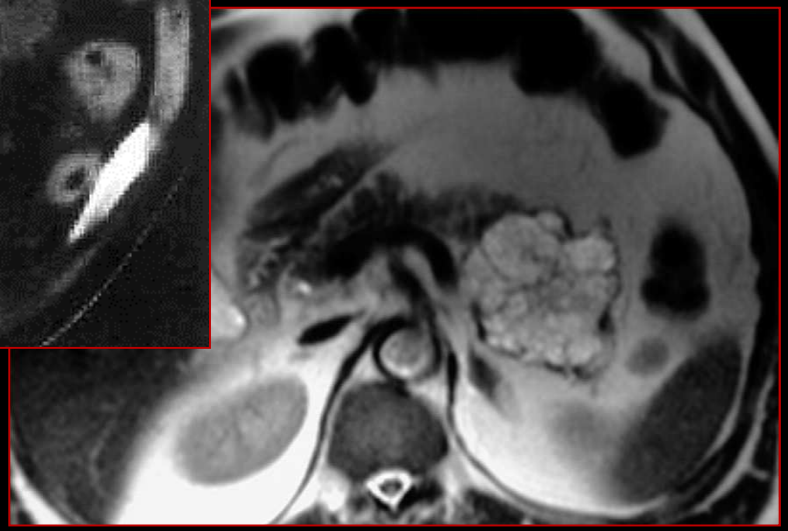
Benigno;
No evoluzione

80% asintomatico
20% sintomatico





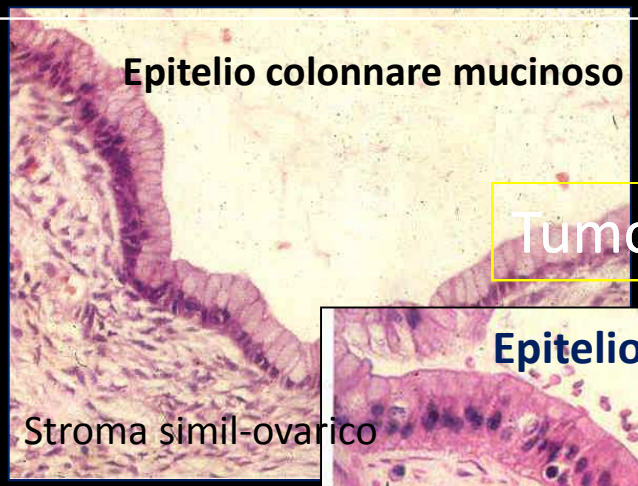
Non comunica con il sistema duttale



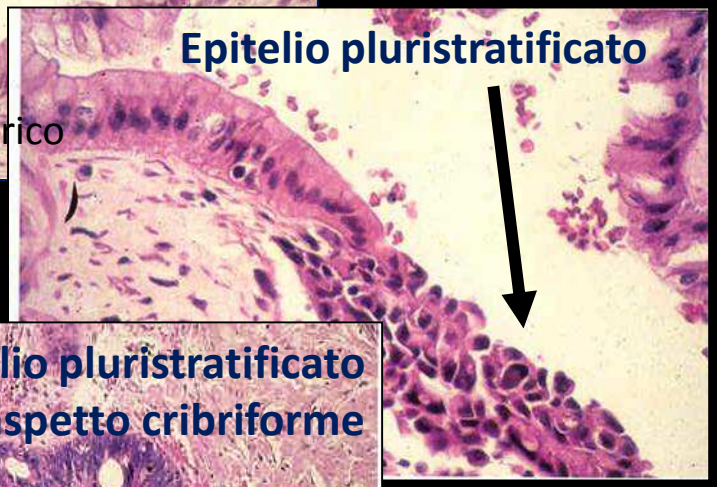
TUMORE CISTICO MUCINOSO

Si evoluzione

Cistoadenoma mucinoso

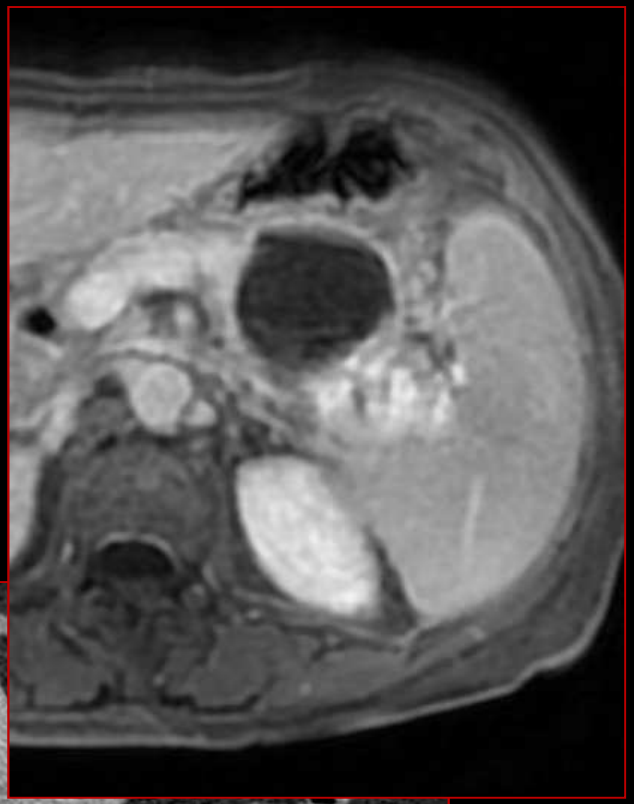


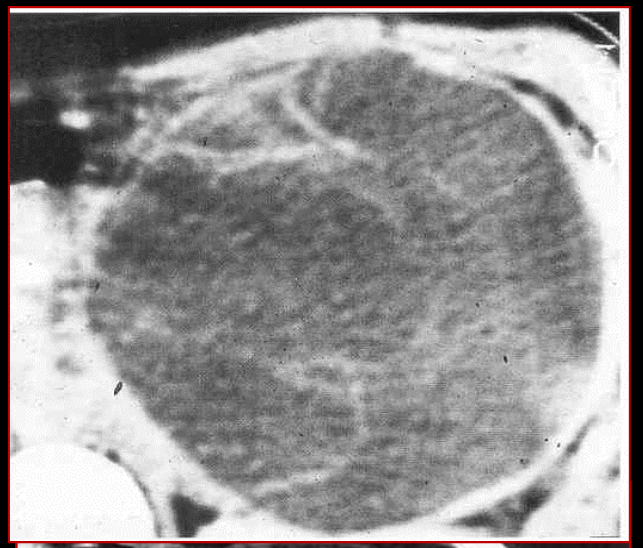
Tumore borderline

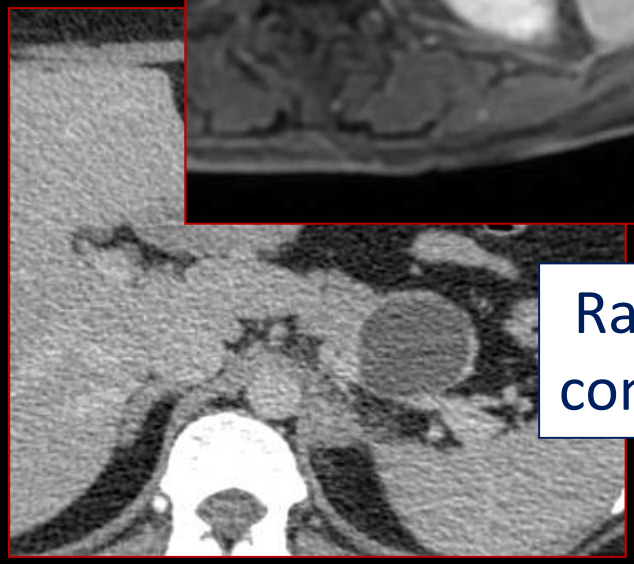


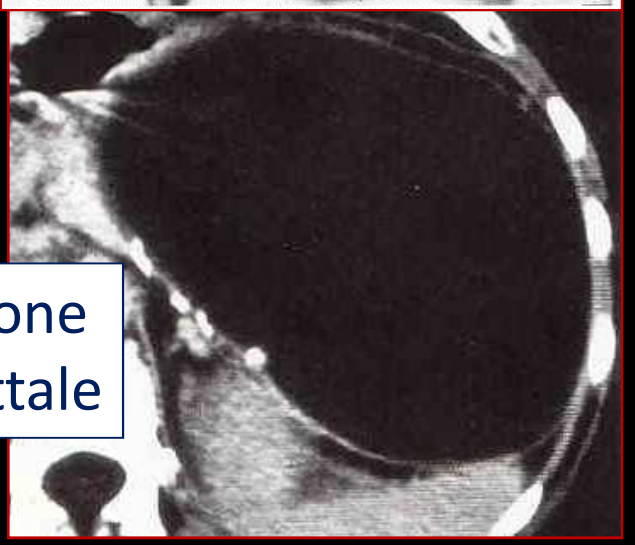
Cistoadenocarcinoma

70% asintomatico
30% sintomatico









Rara comunicazione
con il sistema duttale

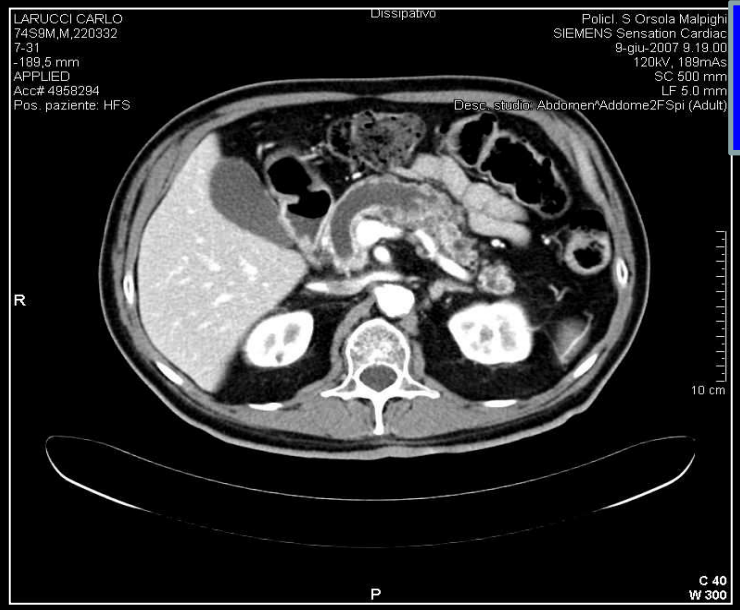
NEOPLASIA PAPILLARE INTRADUTTALE MUCINOSA

traductal papillary mucinous neoplasia

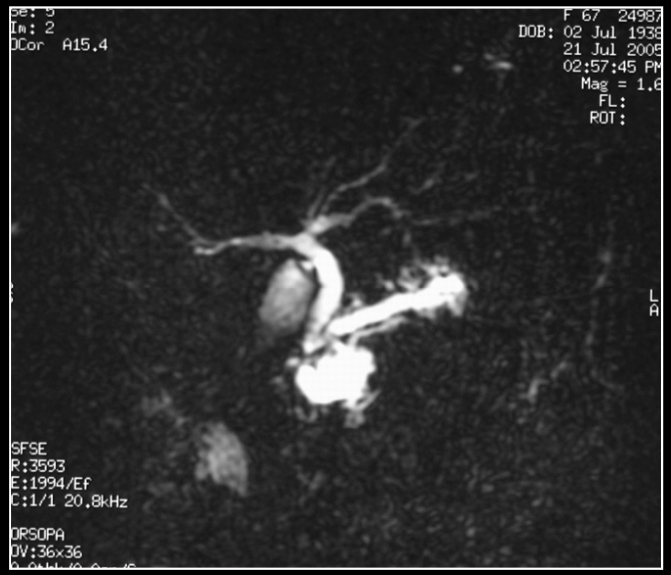
condizione precancerosa
(in quanto tempo evolve ???)

adenoma---------carcinoma

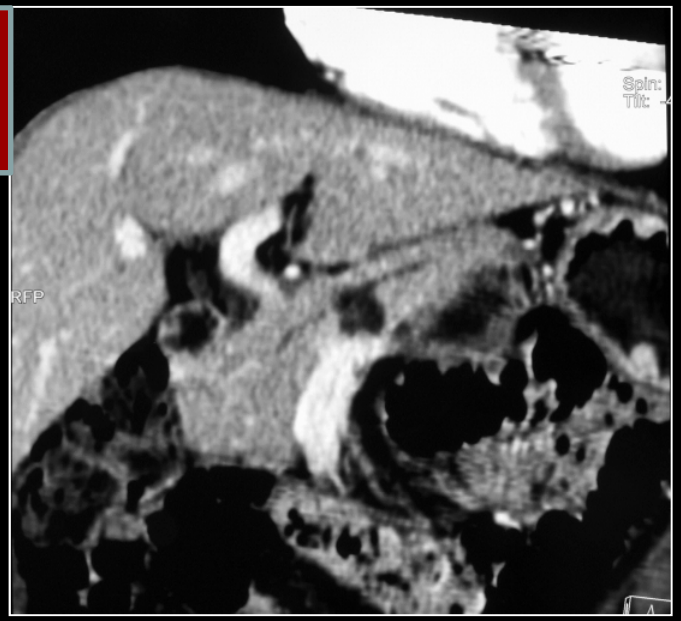
…la stessa storia naturale…??



45%
Main duct



44%
Branch duct



11%
Mixed

…una differente storia naturale…

Main/Mixed duct type

Reference (first author)	Year published	Patients	Malignant including CIS, %	Invasive malignancy, %
Kobari [16]	1999	13	92	23
Terris [17]	2000	30	57	37
Doi [18]	2002	12	83	Not stated
Matsumoto [19]	2003	27	63	Not stated
Choi [20]	2003	34	85	Not stated
Kitagawa [21]	2003	37	65	54
Sugiyama [22]	2003	30	70	57
Sohn [23]	2004	69	Not stated	45
Salvia [24]	2004	140	60	42
Mean of all series			70	43

Tanaka e Coll, 2006

Branch duct type

Reference (first author)	Year published	Patients	Malignant including CIS, %	Invasive malignancy, %
Kobari [16]	1999	17	31	6
Terris [17]	2000	13	15	0
Doi [18]	2002	26	46	Not stated
Matsumoto [19]	2003	16	6	Not stated
Choi [20]	2003	12	25	Not stated
Kitagawa [21]	2003	26	35	31
Sugiyama [22]	2003	32	40	9
Sohn [23]	2004	60	Not stated	30
Mean of all series			25	15

A) Neoplasie mucinose vs non mucinose
Come distinguerle??

Table 2. Key Features of Neoplastic Pancreatic Cysts

	Intraductal Papillary Mucinous Neoplasms	Mucinous Cystic Neoplasms	Serous Cystadenomas
Sex distribution	M = F	F > M	F > M
Historical age of presentation	7th decade	5th to 7th decade	7th decade
Clinical presentation	Incidental, abdominal pain, pancreatitis, symptoms or signs of malabsorption	Incidental, abdominal pain, or palpable mass	Usually incidental, rarely abdominal pain or palpable mass
Morphology/imaging characteristics	Dilated main pancreatic duct or pancreatic duct branches; solid component, if present may suggest malignancy	Unilocular cyst. Septations and wall calcifications may be present. Solid component, if present may suggest malignancy	Microcystic/honeycomb appearance typical. Oligocystic appearance less common
Fluid characteristics	Usually thick	Usually viscous	Thin, if sufficient fluid aspirated from a dominant cyst
Cytology	Stains positive for mucin. Columnar cells with variable atypia; yield <50%	Stains positive for mucin. Columnar cells with variable atypia; yield <50%	Cuboidal cells stain positive for glycogen; yield <50%
Accuracy of cyst CEA (ng/mL)	>192, 0.79 area under curve on receiver operator characteristic*		<5, 67%
Malignant potential	Yes	Yes	No

A Khalid, W Brugge.
Am J Gastroenterology 2007

B) Tumore cistico mucinoso vs neoplasia papillare intraduttale mucinosa Come distinguerle??

Characteristic	MCN	BD-IPMN
Sex (% female)	>95%	~55%
Age (decade)	4th, 5th	6th, 7th
Asymptomatic	~50%	Mostly when small
Location (% body/tail)	95%	30%
Common capsule	Yes	No
Calcification	Rare, curvilinear in the cyst wall	No
Gross appearance	Orange-like	Grape-like
Multifocality	No	Yes
Internal structure	Cysts in cyst	Cyst by cyst
Main pancreatic duct communication	Infrequent	Yes (though not always demonstrable)
Main pancreatic duct	Normal or deviated	Normal, or dilated to >5 mm, suggesting combined type

M Tanaka et al
Pancreatology 2012

Patologie neoplastiche pancreatiche

Entità nosografica	%
Adenocarcinoma duttale	80
varianti del duttale	5
Cistoadenoma sieroso	1
Neoplasia mucinosa cistica (cistoadenoma mucinoso)	1
Neoplasia intraduttale papillare mucinosa	5
Carcinoma a cellule acinari	1
Pancreatoblastoma	1
Neoplasia solida-pseudopapillare	1
Neoplasie neuroendocrine	5

AIOM 2015

Funzioni del sistema Neuro-Endocrino Gastro-Entero-Pancreatico (GEP)

Regolazione del metabolismo dei carboidrati

Controllo della peristalsi

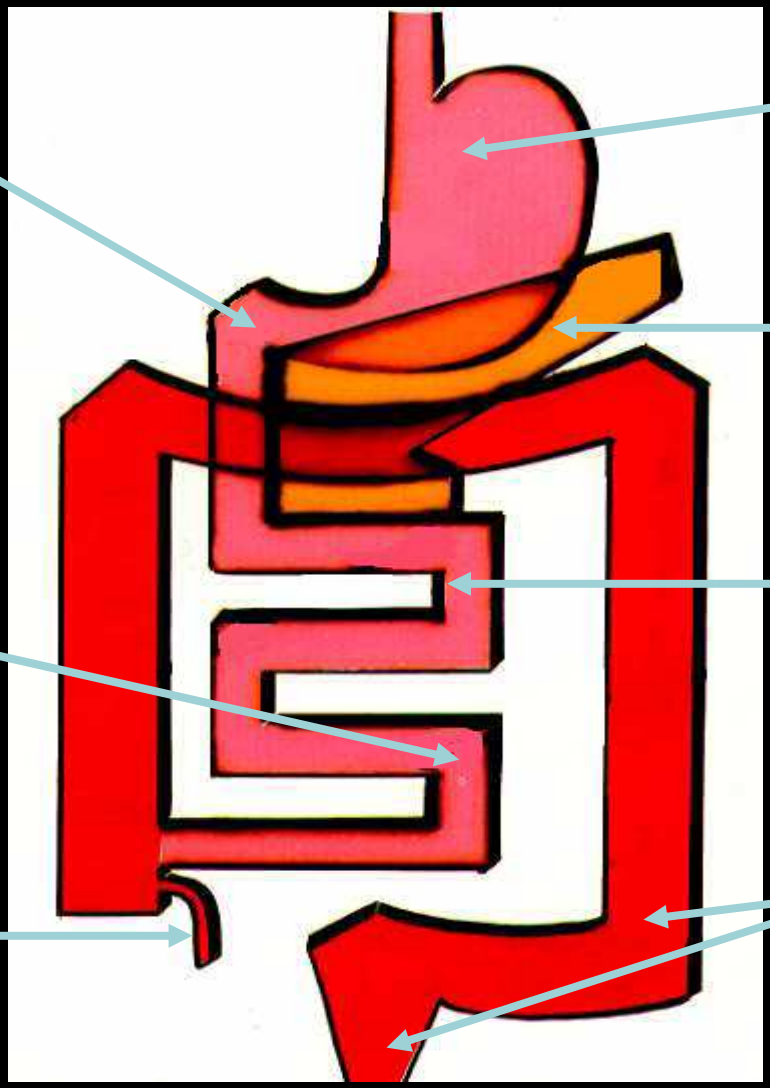
Modulazione della digestione e dell'assorbimento degli alimenti

Controllo del ricambio dell'epitelio gastro-intestinale

Regolazione della secrezione delle ghiandole intestinali

Modulazione del flusso circolatorio

CELLULE NEUROENDOCRINE SISTEMA **GEP**



EC2, D, D1,
G, S, I

ECL, EC1,
D, P, G, X

A, B, D, PP,

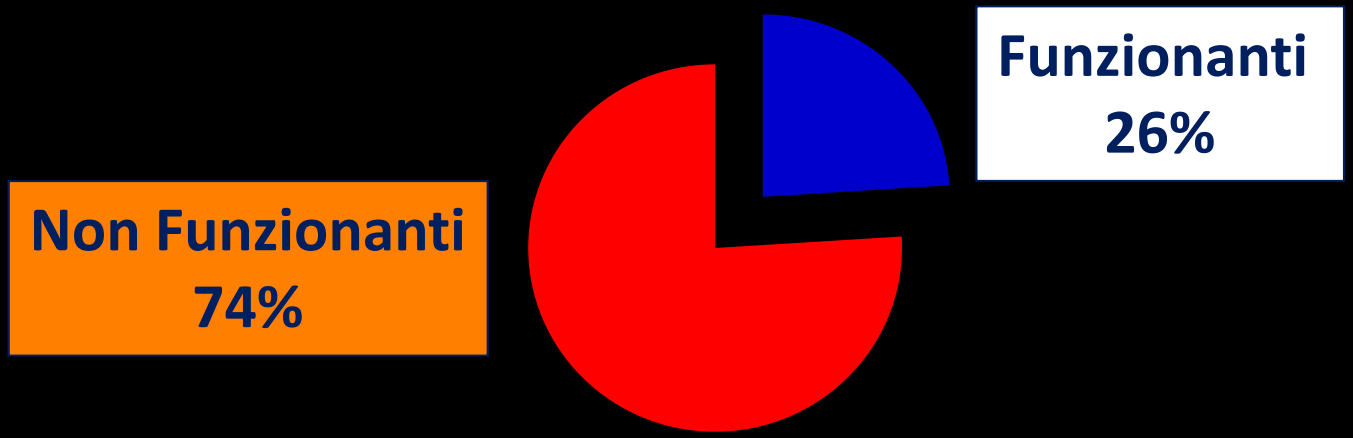
EC1, EC2, D,
D1, S, I, L

EC1, EC2, D
D1, S, I
PP, N, L

EC1, L

EC1, L

TUMORI NEUROENDOCRINI DEL PANCREAS



2010 WHO classification

	NET G1	NET G2	NEC G3
Ki-67 index	<3%	3-20%	>20%
Mitotic count	<2/10 HPF	<2/10 HPF	<2/10 HPF
Differentiation	Well	Well	Poorly

Table 1. F-P-NET syndromes

Name	Biologically active peptide(s) secreted	Incidence (new cases/ 10^6 population/year)	Tumor location	Malignant, %	Associated with MEN-1, %	Main symptoms/signs
Established RFT syndromes (>100 cases)						
VIPoma (Verner-Morrison syndrome, pancreatic cholera, WDHA)	Vasoactive intestinal peptide	0.05–0.2	Pancreas (90%, adult) Other (10%, neural, adrenal, periganglionic)	40–70	6	Diarrhea (90–100%) Hypokalemic (80–100%) Dehydration (83%)
Glucagonoma	Glucagon	0.01–0.1	Pancreas (100%)	50–80	1–20	Rash (67–90%) Glucose intolerance (38–87%) Weight loss (66–96%)
SSoma	Somatostatin	Rare	Pancreas (55%) Duodenum/jejunum (44%)	>70	45	Diabetes mellitus (63–90%) Cholelithiases (65–90%) Diarrhea (35–90%)
GRHoma	Growth hormone-releasing hormone	Unknown	Pancreas (30%) Lung (54%) Jejunum (7%) Other (13%)	>60	16	Acromegaly (100%)
ACTHoma	ACTH	Rare	Pancreas (4–16% all ectopic Cushing's syndrome)	>95	Rare	Cushing's syndrome (100%)
P-NET causing carcinoid syndrome	Serotonin ? Tachykinins	Rare (43 cases)	Pancreas (<1% all carcinoids)	60–88	Rare	Same as carcinoid syndrome above
P-NET causing hypercalcemia (PTHrPoma)	PTHrpP Others unknown	Rare	Pancreas (rare cause of hypercalcemia)	84	Rare	Abdominal pain due to hepatic metastases

TUMORI NEUROENDOCRINI FUNZIONANTI

INSULINOMA - tumore a cellule beta insulari -

-**Sintomi e segni adrenergici**
(ipoglicemia libera catecolamine
tachicardia, sudorazione,
agitazione)
-**Sintomi e segni neuroglicopenici**
(cefalea, disturbi visivi,
disorientamento, confusione,
coma)
Disturbi psichici
(forme persistenti)
Obesità
(forme persistenti)

Esami laboratorio

Ipoglicemia
(a digiuno o dopo sforzo)
Iperinsulinemia
CgA, NSE

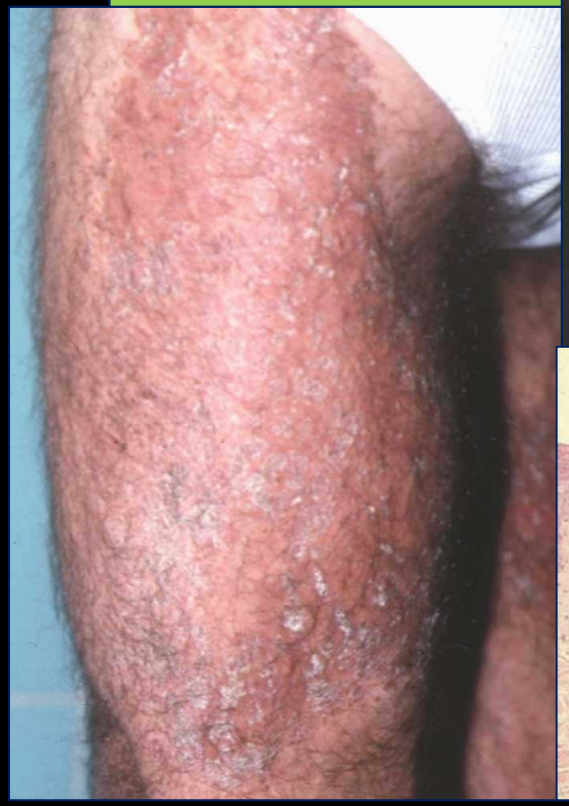
Test del digiuno

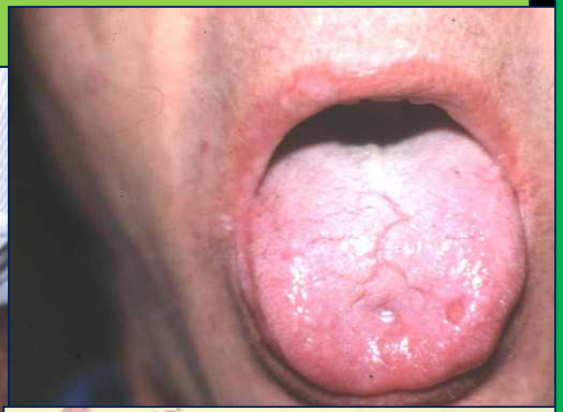
TRIADE DI WHIPPLE
1) IPOGLICEMIA A DIGIUNO
O DOPO SFORZO <40 MG/DL
2) SOLLIEVO DOPO GLUCOSIO EV
3) SINTOMI DA IPOGLICEMIA

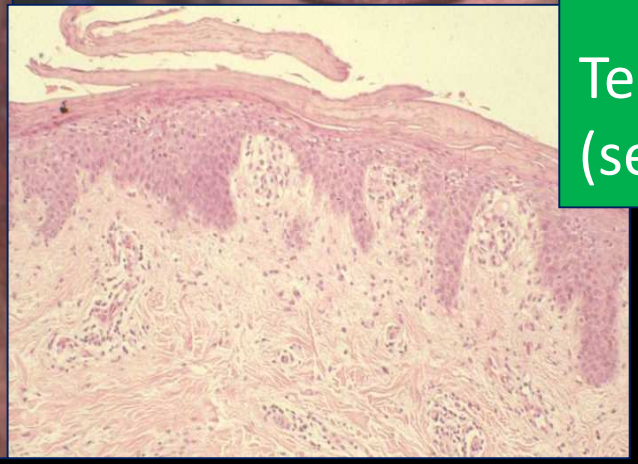
TUMORI NEUROENDOCRINI FUNZIONANTI

GLUCAGONOMA - tumore a cellule alfa insulari -

Diabete mellito
(poliuria e polidipsia)
Eritema necrolitico migrante
Glossite







Esami laboratorio

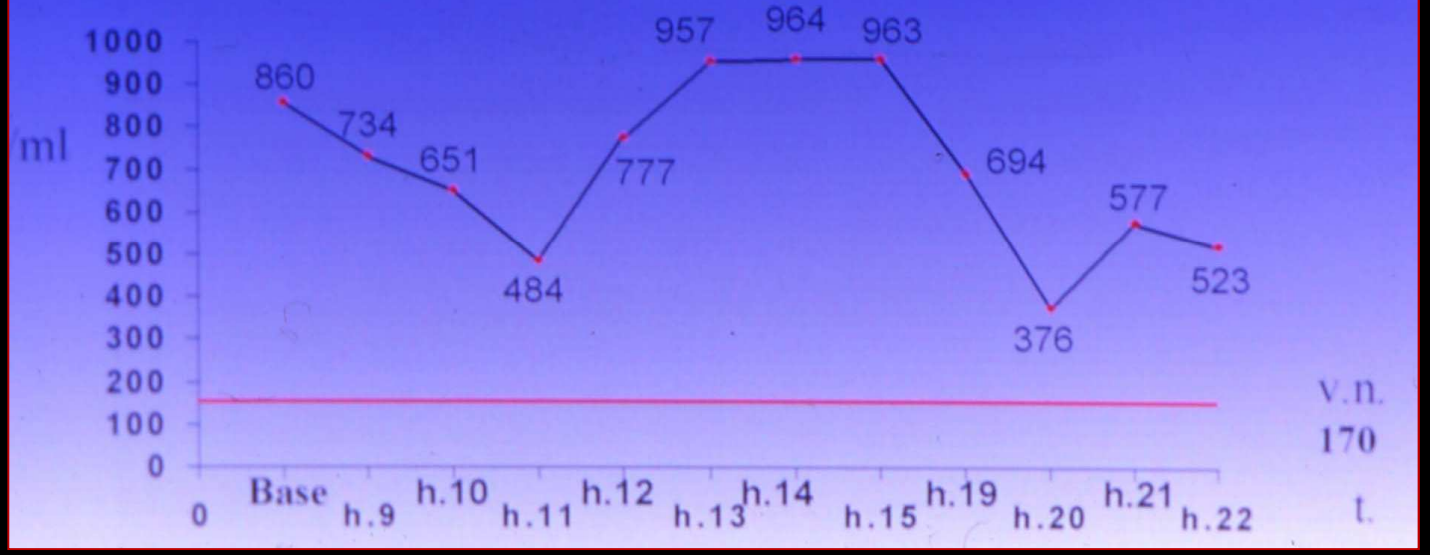
Iperglicemia
Iperglucagonemia
CgA, NSE

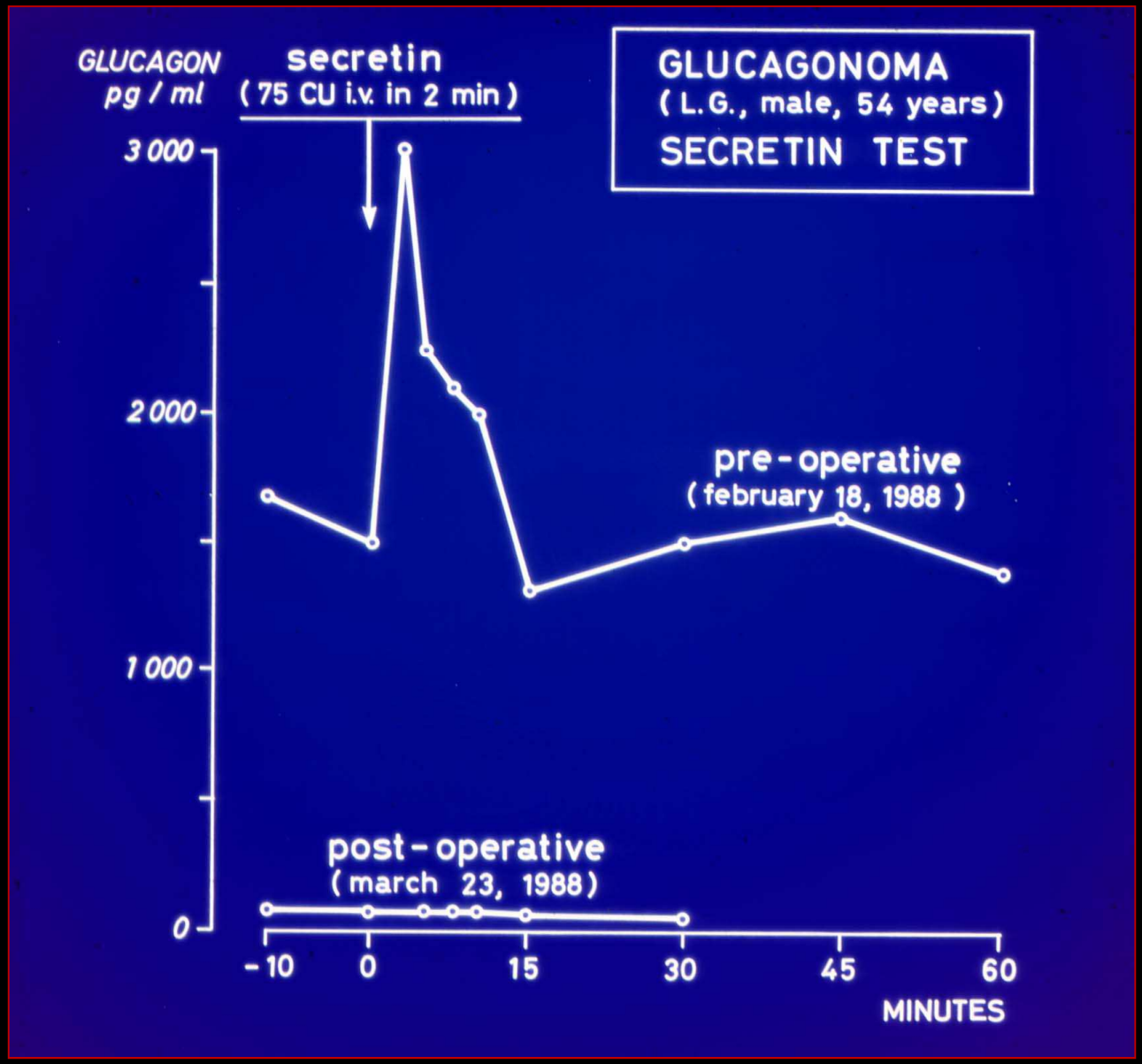
Test stimolo glucagone
(secretina)

„Gino - Gennaio 1995

GLUCAGONEMIA

RITMO CIRCADIANO




GLUCAGON
pg / ml
secretin
(75 CU i.v. in 2 min)
GLUCAGONOMA
(L.G., male, 54 years)
SECRETIN TEST
3 000
2 000
1 000
0
pre - operative
(february 18, 1988)
post - operative
(march 23, 1988)
- 10
0
15
30
45
60
MINUTES

TUMORI NEUROENDOCRINI FUNZIONANTI

GASTRINOMA – cellule G secernente gastrina -

ipersecrezione gastrina

↓ Stimolo cellule ossintiche stomaco

ipersecezione HCl

↓

Ulcere peptiche stomaco, duodeno, tenue

Dolore epigastrico
Pirosi
Diarrea
Reflusso GE
(S. di Zollinger-Ellison)

Esami laboratorio

BAO, MAO
pH gastrico
Gastrinemia
CgA, NSE

Test stimolo gastrina(secretina)

TUMORI NEUROENDOCRINI FUNZIONANTI

SOMATOSTATINOMA – a cellule delta insulari -

diabete mellito inibizione della secrezione insulinica
colelitiasi per l'inibizione della secrezione di colecistochinina,
steatorrea per l'inibizione della secrezione di colecistochinina e secretina
ipocloridria per l'inibizione della secrezione acida a livello gastrico tramite soppressione della produzione di gastrina.

VIPoma

- fecal osmotic gap: 290-[(stool Na^+ level + stool K^+ level) x2] < 50 mOsm → secretory diarrhea

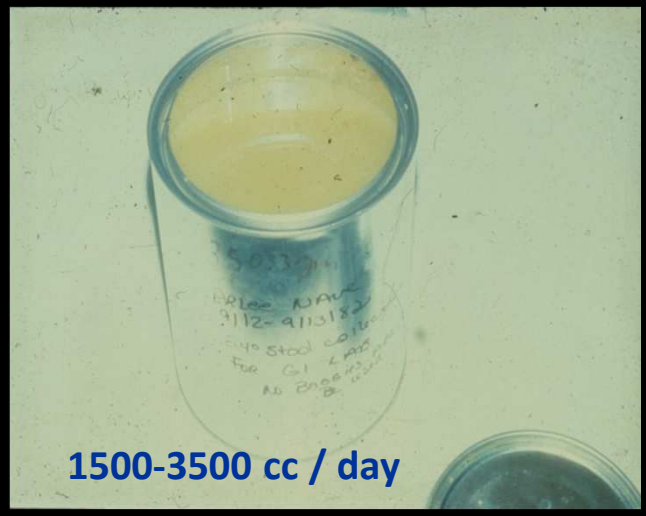
  (> 125 mOsm → osmotic diarrhea)

- ↓↓↓ K^+, with high volume diarrhea and weight loss → NET

- VIP-oma or Verner-Morrison syndrome or "WDHA"

  (*watery diarrhea*, *hypokaliemia*, *achlorhydria*)

	Stool weight (g/24h)	[VIP] plasma n.v. <150 pg/ml
On diet	3504	1100
Fasting	1696	1050
Octreotide (500 µg s.c. b.i.d)	244	200



Modlin et al., Lancet Oncol, 2008; 9(1):61-72

Semeiotica strumentale

I livello

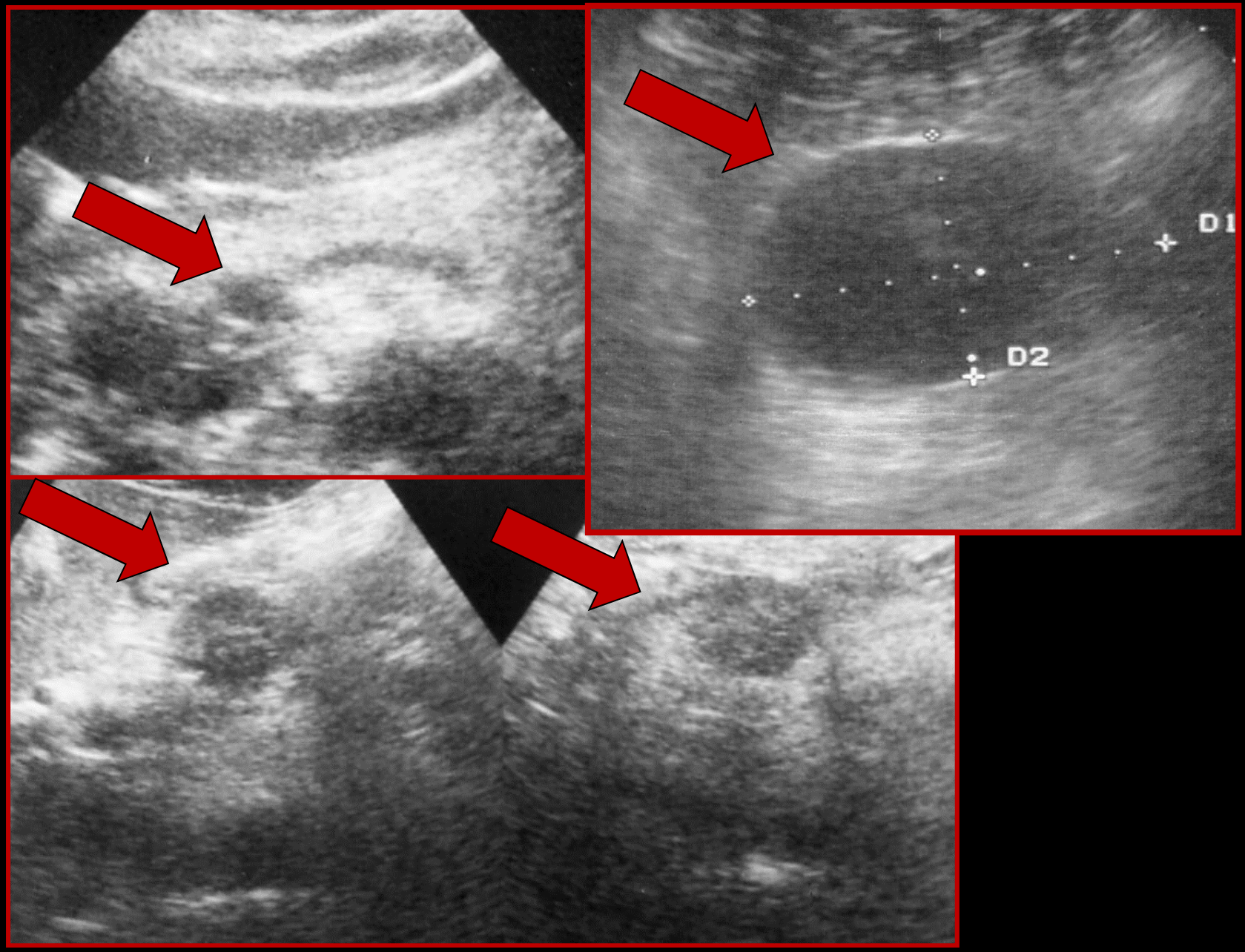
Ecografia senza e con mdc

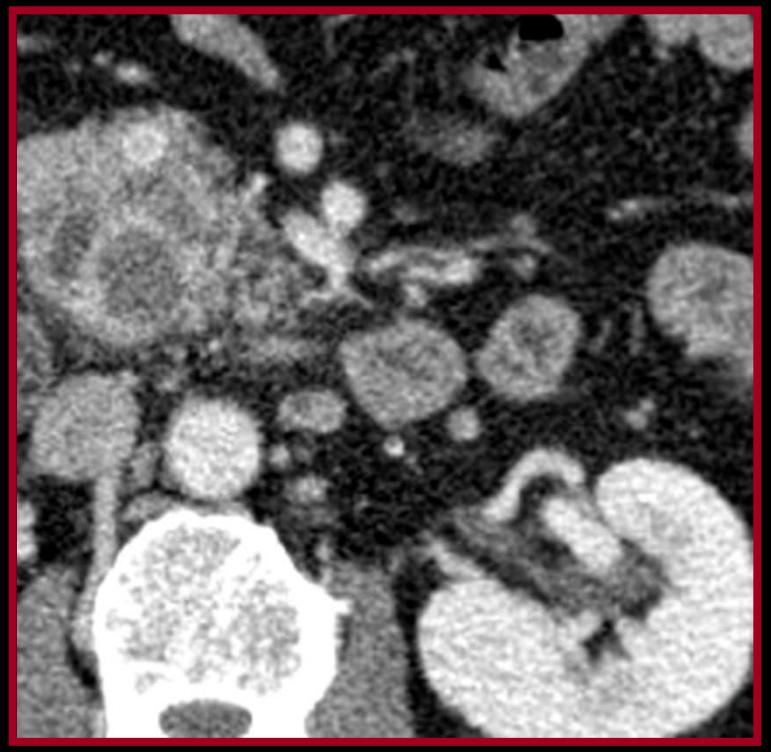
TC multidetettore toraco addominale

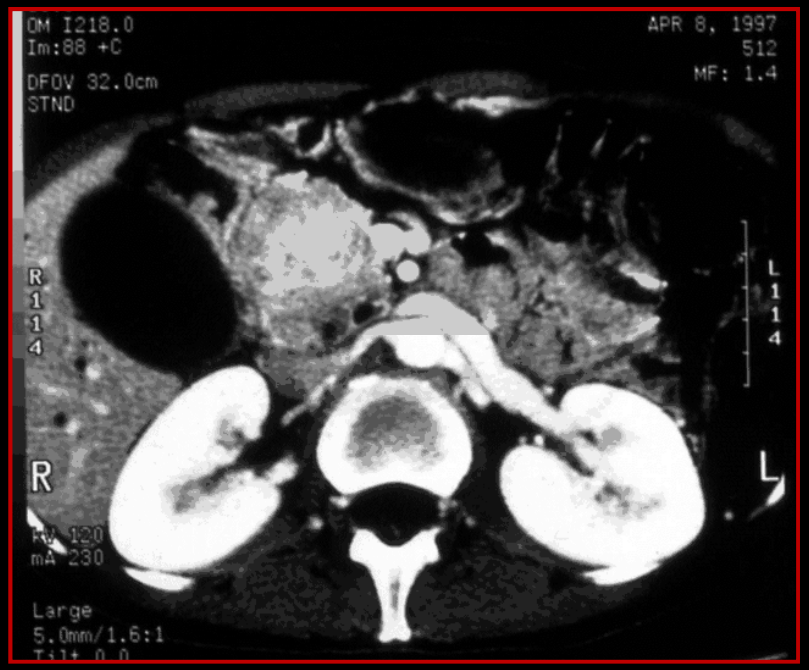
Diagnosi di massa pancreatica sospetta

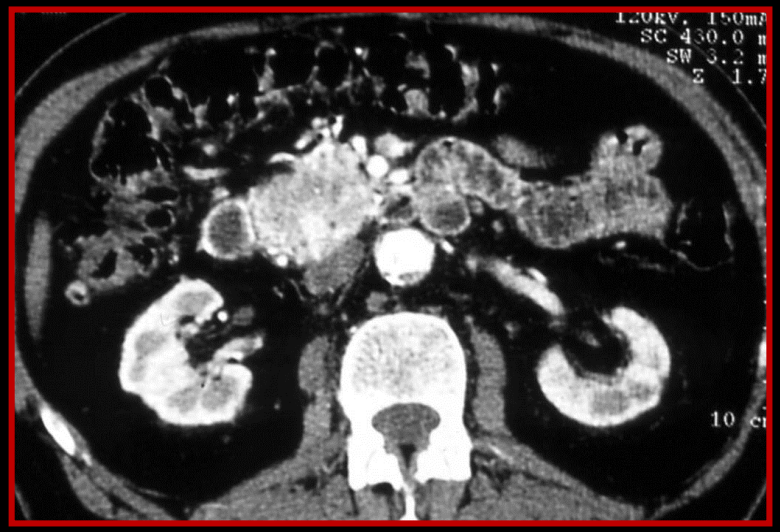
Stadiazione clinica cTNM

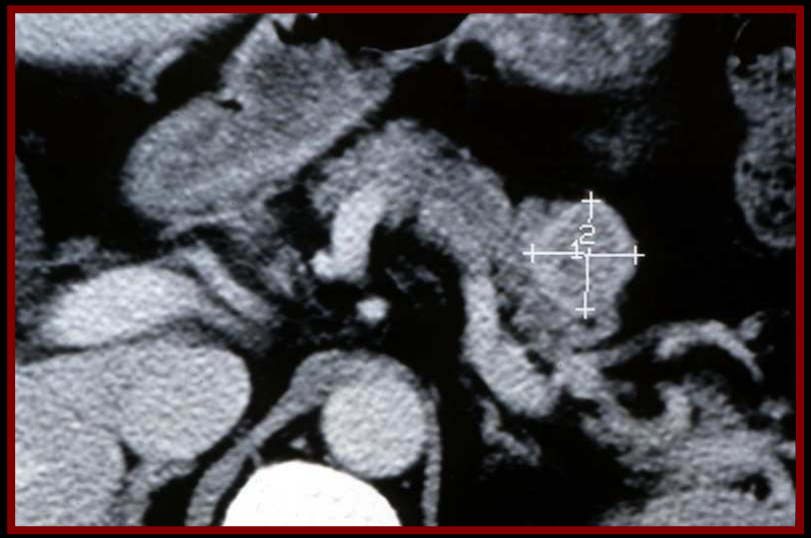
Criteri di resecabilità


D1
D2




OM I218.0
Im:88 +C
APR 8, 1997
512
DFOV 32.0cm
STND
MF: 1.4
R 1 1 4
L 1 1 4
R
L
kV 120
mA 280
Large
5.0mm/1.6:1


120KV, 150mA
SC 430.0 m
SW 5.2 m
Z 1.7
10 c


2.2

Limited to the pancreas, ≤2 cm in greatest dimension	NA
Limited to the pancreas, >2 cm in greatest dimension	NA
Beyond the pancreas but without involvement of the superior mesenteric artery	NA
Involvement of celiac axis or the superior mesenteric artery (unresectable tumor)	NA
	NA
	NA

cTNM

T definition	
T1	Limited to the pancreas, <2 cm
T2	Limited to the pancreas, 2–4 cm
T3	Limited to the pancreas, >4 cm or invading duodenum or bile duct
T4	Tumor invading adjacent organs (stomach, spleen, colon, adrenal gland) or the wall of large vessels (celiac axis or the superior mesenteric artery)

Long-term survival rates
- post resection