Ecoendoscopy in children: an update on indications and clinical usefulness

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Rome, 13th April 2013

PEDiatric GASTROINTESTINAL endoscopy AND BEYOND
**INSTRUMENTATIONS**

Endoscopy is combined with ultrasound, by placing the US transducer on the tip of an endoscope, to obtain images of the internal organs in the chest and abdomen.

Electronic probes may be oriented radially or linearly. Echoendoscopes operate from 5 to 20 MHz, permitting a spectrum of depth of penetration and image resolution.

Miniprobes can be inserted inside the biopsy channel of a standard endoscope.
Radial EUS scopes provide a $360 \, ^\circ$ sonographic view, which is perpendicular to the tip of the endoscope.

Endoscopic view is frontal or side view.
Linear EUS scopes provide a 150° sector view, which is parallel to the long axis of the endoscope.

Linear EUS can be used to perform fine needle aspiration (FNA) and other interventional procedures, first introduced by Vilmann in 1992.
Fine Needle Aspiration

All accessible EUS lesions which need to be cytologically defined, if no other easier or accessible technique can be utilized.

Palazzo L 2003 Quelles sont les indications reconues de la ponction sous echoendoscopie? Acta endoscopica 1:17-29

Single use needle are inserted in the biopsy channel and it has a 4-layer configuration:

- a) a handle assembly for controlled advancement of the needle with a dedicated port for the needle stylet and an attachment for a vacuum syringe;
- b) a semi-rigid protective sheath
- c) a hollow needle that may come in one or more size
- d) a stylet to avoid perforation of the spiral and damage of the working channel.
FNA needles are available in 19, 22, and 25 gage size.

Diagnostic FNA are 22 or 25 gage sizes.

25G, the finest one, can be used to perform FNA of highly vascularized mass such as nodes; it is also preferred unless there are reasons to use bigger needles.

19G needle

Larger core histological needle are needed when acquisition of pathological specimen is required rather than cytological or for therapeutic procedure.
The EchoTip ProCore needles obtain intact tissue samples, allowing for a histological diagnosis rather than conventional cytological diagnosis based on individual cells.

It has a handle with a spring loaded shot mechanism to facilitate the penetration of the needle into the lesion allowing more efficient tissue samples to be obtained.
FNA seems to be a safe and efficient procedure even in paediatric age, despite the use in paediatric population remains limited.

EUS anatomy from stomach

wirsung

wirsung
EUS anatomy from duodenum

Common bile duct
### Diagnostic EUS indications

#### Primary indications
- Tumoral GI wall staging, local nodes FNA
- Differential diagnosis for submucosal lesions (FNA?)
- Diagnosis and staging of bilio-pancreatic tumors, local nodes FNA
- Diagnosis of choledochal lithiasis
- Staging of lung tumors, local nodes FNA

#### Secondary indications
- Portal Hypertension evaluation
- Diagnosis of chronic pancreatitis
- Diagnosis of ascites
- Barrett’s esophagus evaluation?

### Therapeutic EUS indications

#### Primary indications
- Drainage of pancreatic pseudocyst
- Celiac plex neurolysis

#### Secondary indications
- Pancreatic tumor ablation
- Bilio-pancreatic anastomosis
INDICATIONS in CHILDREN


Upper digestive tract  EUS was performed in children suffering from biliopancreatic diseases, angiomatosis or digestive tumors

Anorectal EUS  investigated tumors (adenomas and carcinoid tumor) or proctological diseases
INDICATIONS:

Pancreatobiliary EUS:
pancreatitis, solid pancreatic mass, cystic pancreatic mass, cyst in the setting of chronic pancreatitis, suspected annular pancreas, celiac plexus block, suspected CBD stone, abdominal pain and atrophic pancreas, ampullary adenoma, abnormal MRCP in a patient with jaundice.

Gastric EUS:
mucosal lesions, subepithelial lesions

Mediastinal EUS:
mediastinal masses/lymph nodes.

Other indications:
esophageal stricture, unexplained abdominal pain, unexplained abdominal pain with celiac axis block, perirectal fluid collection
Indications for EUS in children were similar to those for adults, but children have a much lower incidence of neoplastic diseases.

**TABLE 1. Indications for EUS**

<table>
<thead>
<tr>
<th>Indication</th>
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<tbody>
<tr>
<td>Upper abdominal pain of suspected pancreatobiliary origin</td>
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<td>Pancreatitis (acute, recurrent)</td>
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<td>Abnormal pancreatic imaging (CT/MRI)</td>
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<td>Mucosal/submucosal lesions</td>
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<td>Suspected biliary obstruction</td>
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<tr>
<td>Celiac plexus block</td>
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<tr>
<td>Unexplained rectal pain/bleeding</td>
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<tr>
<td>Suspected perianal fistulas/fecal incontinence</td>
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<td>Pancreatic duct puncture for ductography during ERCP</td>
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</tbody>
</table>
Disorders of the pancreatobiliary system were the primary indication.

Impact of EUS in the evaluation of pancreaticobiliary disorders in children
Shyam Varadarajulu, MD, C Mel Wilcox, MD, Mohamad A Eloubeidi, MD, MHS
Birmingham, Alabama, USA

Pediatric pancreatic EUS-guided trucut biopsy for evaluation of autoimmune pancreatitis
Larissa L. Fujii, MD,† Suresh T. Chari, MD,‡ Mounif El-Youssef, MD,§ Naoki Takahashi, MD,∥
Mark D. Topazian, MD,† Lizhi Zhang, MD,∥ Michael J. Levy, MD†

Utility of EUS-guided FNA in the Management of Children With Idiopathic Fibrosing Pancreatitis
*James L. Buxbaum, †Mohamad A. Eloubeidi, and ‡Shyam Varadarajulu
Case Report

EUS-FNA for a Pancreatic Neuroendocrine Tumor in a Four-Year-Old Daughter of a Woman Exposed to Radiation at Chernobyl

Case Reports in Gastrointestinal Medicine 2012

Jesse Lachter,1 Marc S. Arkovitz,2 Sergey Postovski,3 Julian M. Waldner,4 Ron Shaoul,1 Offir Ben Ishay,5 and Yoram Kluger5

The Use of Endoscopic Ultrasound in the Diagnosis of Solid Pseudopapillary Tumors of the Pancreas in Children

Journal of Pediatric Surgery, 2002; 37(9):1370-1373

By Evan P. Nadler, Anna Novikov, Brian R. Landzberg, Mark B. Pochapin, Barbara Centeno, Thomas J. Fahey, and Nitsana Spigland

Pancreatic cystic lymphangioma in a 6-year-old girl, diagnosed by endoscopic ultrasound (EUS) fine needle aspiration

Endoscopy 2011; 43: E61-E62
Therapeutic EUS indications

Endoscopic Ultrasound–guided Drainage of Pancreatic Fluid Collections in Children

Jayapal Ramesh, Ji Y. Bang, Jessica Trevino, and Shyam Varadarajulu

Efficacy of Endoscopic Ultrasound-Guided Drainage of Pancreatic Pseudocysts in a Pediatric Population

Saad F. Jazrawi · Bradley A. Barth · Jayaprakash Sreenarasimhaiah

Infants and children (0-15 years) with typical symptoms of GERD persisting after a 14-days proton pump inhibitor trial were included in a prospective study protocol. Upper endoscopy and EUS of the esophageal wall were performed.
The Role of Endoscopic Ultrasound for Evaluating Portal Hypertension in Children Being Assessed for Intestinal Transplantation

Patrick J. McKiernan, Khalid Sharif, and Girish L. Gupte

Surgery or endoscopy to treat duodenal duplications in children

Erminia Romeo, Filippo Torroni, Francesca Foschia, Paola De Angelis, Tamara Caldaral, Maria Rita Santi, Giovanni Federici di Abriola, Romina Caccamo, Lidia Monti, Luigi Dall'Oglio

Journal of Pediatric Surgery (2011) 46,
Endoscopic Ultrasound to Guide the Combined Medical and Surgical Management of Pediatric Perianal Crohn's Disease

EUS-guided fistulization of postoperative colorectal stenosis in an infant with Hirschsprung’s disease: a new technique.

Everson L. A. Artifon, MD, PhD, FASGE; Flávio Ferreira, MD, Renato Baracat, MD, Luciano Okawa, MD, MSc, Kapil Gupta, MD, MPH, Paulo Sakai, MD, PhD, FASGE, Manoop S. Bhutani, MD, FASGE, FACG, FACP, AGAF
PERSONAL INDICATIONS in CHILDREN

upper EUS
- suspected choledocholithiasis,
- abnormal biliary ductal system
- acute or recurrent pancreatitis
- abdominal pain suggestive of pancreatobiliary origin
- abdominal trauma
- pancreatic cyst/mass
- lymphoma

lower EUS
- suspected anal fistula
- follow-up after fistulectomy surgery
- fecal incontinence
More than 60% of ERCPs done in children are diagnostic with a complication rate of 2.5% to 11%. EUS appears to be a logical alternative.

The diagnostic accuracy of EUS in the evaluation of PB disorders, such as choledocholithiasis, chronic pancreatitis, and pancreaticobiliary malignancies, exceeds 90% (95-100%).

Evaluation of pancreaticobiliary disorders is the most common indication for EUS referrals in a pediatric population (choledocholithiasis and idiopathic or recurrent pancreatitis).

CLINICAL USEFULNESS of EUS

Pancreaticobiliary disorders

Evaluation of pancreaticobiliary disorders is the most common indication for EUS referrals in a pediatric population (choledocholithiasis and idiopathic or recurrent pancreatitis).

More than 60% of ERCPs done in children are diagnostic with a complication rate of 2.5% to 11%. EUS appears to be a logical alternative.
A new diagnosis was provided by EUS in 86% of patients.

It precluded the need for ERCP in the majority (65%) of patients. EUS supplanted ERCP in 84% of cases.

EUS had an impact on patient management in 93% of cases:
- established new diagnosis,
- precluded need for ERCP,
- provided additional information that facilitated focused endotherapy


Attila T, Adler D, Hilden K et al: EUS in pediatric patients. GASTROINTESTINAL ENDOSCOPY 2009;70 (5):892-8

Choledocholithiasis in adults

EUS
higher accuracy than CT and US.

Similar to MRI but
EUS seems to be superior for small stones (<3mm)

Sensibility 84-100%
Specificity 96-100%

It precluded the need for ERCP in 60-75%

US and serological tests
low sensibility.

Choledocholithiasis
EUS is useful to determine the cause (especially if lithiasis)

Sensibility 68% - 100%
Specificity 78%-97%
Accuracy 32-88%

Seicean A. Endoscopic ultrasound in chronic pancreatitis: where we are? World J Gastroenterol 2010
CHRONIC PANCREATITIS
CHRONIC PANCREATITIS
Drainage of pancreatic cyst

The common causes of pancreatic fluid collections (PFCs) in children worldwide are trauma (leading cause up to 50% of cases), gallstone, idiopathic, hereditary, viral, or toxin-mediated pancreatitis.

Conservative management:
PFCs < 6 cm.

Therapeutic/surgical intervention:

- PFCs ≥ 10 cm,
- that become symptomatic,
- persist for ≥ 6 weeks,
- continue to increase in size

Pseudocysts the most common cystic lesion in childhood, about 75% of all cases

Nonoperative failure rate of 26% to 33%
(the risk of spontaneous rupture)
Surgical mortality rate of 0-10% and morbidity rate 11-35%,
In the last years, endoscopic drainage of pseudocysts in adults has evolved towards EUS guided drainage to identify the location of the cyst, potentially intervening blood vessels, and the optimal site for puncture and subsequent stent placement.

EUS compared to gastroscopy for transmural drainage of pseudocysts, the rates of technical success were significantly better for the EUS-guided approach with even minor complications.

Surgical cystogastrostomy compared to EUS guided drainage: clinical outcomes were comparable, but patients treated with EUS had a significantly better quality of life, shorter length of hospital stay, the technique was less costly.


It has been shown in a pediatric population that a persistent pseudocyst exceeding 6 cm in size will require a drainage procedure.

Single-step EUS-guided cyst-gastrostomy has a technical success rate of 94%, with longterm pseudocyst resolution in 85% of cases.

Single-step EUS-guided drainage is a minimally invasive, safe, and a highly effective technique for the management of symptomatic PFCs in children.

Immediate complications

- bleeding (1%)
- perforation (1%)

Procedure-related infection 5%
(diminished by use of prophylactic antibiotics)

Long-term complications (15-24%)

- stent migration
- delayed cyst infection
- pseudocyst recurrence

Jazrawi S, Barth B, Sreenarasimhaiah J
Efficacy of Endoscopic Ultrasound-Guided Drainage of Pancreatic Pseudocysts in a Pediatric Population
Mucosal/submucosal lesions

Although the incidence of subepithelial lesions in the pediatric population is not known, its incidence in the general population is 0.4% in diagnostic endoscopies.

Diagnostic yield of EUS by sonographic criteria

71%–84% in children


Attila T, Adler D, Hilden K et al EUS in pediatric patients GASTROINTESTINAL ENDOSCOPY 2009;70 (5):892-8
Pediatric mediastinal masses are a heterogeneous group of asymptomatic or potentially life-threatening congenital, infectious, and neoplastic diseases.

EUS can both identify and guide FNA of mediastinal nodes as small as 5 mm.

EUS sensitivity for lymphoma 73% to 80%.

Attila T, Adler D, Hilden K et al. EUS in pediatric patients. GASTROINTESTINAL ENDOSCOPY 2009;70(5):892-8

ASGE guidelines Role of EUS for the evaluation of mediastinal adenopathy Gastrointest endosc 2011
EOSINOPHILIC ESOPHAGITIS

A significant increase in esophageal mucosal layer both in the distal and in mid-esophagus as compared to GERD and controls.

No difference between GERD and controls, suggesting that the increase in mucosal thickness is unique to EE.

PORTAL HYPERTENSION

EUS is superior to upper endoscopy for detecting gastro-esophageal varices in children with intestinal failure-associated liver disease and results in fewer liver biopsies being necessary.


Congenital esophageal stenosis

3 types:
- the presence of ectopic tracheobronchial tissue (TBR),
- the presence of a membranous diaphragm (MD),
- segmental hypertrophy of the muscularis and submucosal layers with diffuse fibrosis (FMH) treated by bougienage or dilatation

EUS has been found to be a useful imaging technique in the evaluation of mucosal and submucosal lesions


EUS has the advantage that it may be done at the same time as colonoscopy in the hands of gastroenterologist. Rectal EUS is feasible in the pediatric population, and guided which patients were referred for surgical evaluation and seton placement, as well as the timing of seton removal. EUS also accurately identified patients who did not require surgical referral.

Rosen MJ, Moulton DE, Koyama T et al Endoscopic Ultrasound to Guide the Combined Medical and Surgical Management of Pediatric Perianal Crohn’s Disease. Inflamm Bowel Dis. 2010
Rectal and anal disease

EUS evaluation of perirectal and perianal complications of Crohn's disease has been demonstrated to be superior to fistulography, CT, and equal to or superior to MRI.

Accuracy: EUS 91%; MRI 87%; examination under anaesthesia 91%. In addition, a combination of any of the imaging modalities with examination under anaesthesia provided 100% accuracy in these patients.


EUS results influenced patient management in 86% of the patients

The major difference when performing EUS in children and in adult patients is the type of anesthesia administered: general anesthesia in children for invasive procedures is needed.

The procedure is safe, with a reported complication rate of less than 1%.

CONCLUSIONS....QUESTIONS??

✓ small number of patients
✓ the important role of an adult gastroenterologist in the management of the pediatric population
✓ adults instrumentations
EUS and EUS-FNA are safe procedures, and affect management of PB disorders in children.

EUS could replace ERCP as a diagnostic tool for evaluation of most pancreatobiliary disorder

Feasible applicability and safety of EUS with or without FNA for pediatric patients using echoendoscopes designed for use in adults

More studies are needed and more pediatric gastroenterologist need to be trained
Thank you for the attention!
PERSONAL CLINICAL USEFULNESS in CHILDREN

**upper EUS**

confirmed choledocolithiasis and sclerosing cholangitis (100%)

in 1 of the 4 patients with recurrent pancreatitis EUS was completely normal and in 3 patients EUS showed initial chronic pancreatitis treated symptomatically; in all 3 patients with abdominal pain suggestive of PB origin, EUS showed pancreatitis signs with gallbladder sludge and microlithiasis (<3mm) not reported at the US; in patient with abdominal trauma EUS

**lower EUS**

..............
ROSEMONT CLASSIFICATION

Criteri Major e minor

A

B

Diagnosi è “consistent”:

- 1 major A + ≥ 3 minor
- 1 major A + 1 major B
- 2 major A

Per migliorare l’accuratezza:

Somministrazione di secretina

Utilizzo del contrasto

Elastosonografia

Pancreatite cronica
Pancreatite cronica
Calcolosì coledoco
Calcolosi coledoco
Calcolosì della colecisti

Macrocalcolo

Sludge
Patología anal

>70% delle lesioni cistiche del pancreas
4 settimane dopo un episodio di pancreatite acuta, e/o trauma addominale
Contenente materiale necrotico e senza strato epiteliale

MD Morgan. Cystic lesions of the pancreas. Sminars in Gastroenterology
G Garcea, A rajesh, CP Neal et al. Cystic lesions of the pancreas. Pancreatology 2008;8:236-51
CISTOADENOMA SIEROSO

Più frequente nelle donne (ratio 2:1), settima decade

Asintomatico

Solitamente nella testa pancreatica

Cicatrice stellata centrale con possibili calcificazioni (10-30%)

Nessuna comunicazione con il dotto pancreatico principale

Benigno (rischio di malignità 3%)

MD Morgan. Cystic lesions of the pancreas. Seminars in Gastroenterology
G Garcea, A rajesh, CP Neal et al. Cystic lesions of the pancreas. Pancreatology 2008;8:236-51
Adenoma microcistico sieroso (SMA)

Adenoma macrocistico sieroso

Cisti associate alla sindrome di Von Hippel-Lindau (VHL) (50-80% pz presenta cisti pancreatiche),

Cistadenocarcinoma sieroso

Roggin KK, Chennat J, Oto A, et al. Pancreatic cystic neoplasm

CISTOADENOMA MUCINOSO

Più frequente nelle **donne** (ratio 9:1), quinta-sesta decade

Lesioni solitarie, solitamente nel **corpo-coda**

Nessuna comunicazione con il dotto pancreatico principale (o microcomunicazioni?)

Lesione **premaligne**, quindi richiede resezione chirurgica

**Meno del 20%** sono invasivi, i non invasivi si classificano in base al grado di displasia epiteliale (bassa, media, alta)

Presenza di aspetto di tipo “**stroma ovarico**”


MD Morgan. Cystic lesions of the pancreas. Smeinars in Gastroenterology.

G Garcea, A rajesh, CP Neal et al. Cystic lesions of the pancreas. Pancreatology 2008;8:236-51

Prasad S et al Endoscopic ultrasound of pancreatic cystic lesions. ANZ J Surg. 2010
Tumore Mucinoso Intraduttale Papillare

Descritto nel 1982

Rapporto maschi/femmine 2:1

6-7° decade

Prevalentemente testa del pancreas

Eccessiva produzione di muco con accumulo nei dotti che si diltano, fuoriuscita di muco dalla papilla.

Lesione pre-maligna/maligna (5-7 anni per divenire invasiva)

Gourgiotis S, Ridolfini MP, Germanos S. Intraductal papillary mucinous neoplasms of the pancreas. EJSO 2007
**classificazione**

**MAIN DUCT TYPE:**
diffusa o parziale dilatazione del dotto pancreatico principale specie nella testa

**SIDE BRANCH TYPE:**
interessa uno o più dotti periferici. Solitamente in pazienti più giovani e con un minor potenziale maligno

**COMBINATO:**
una combinazione del main duct type e branch type
Segni di malignità

Dotto pancreatico principale >1-1,5 cm
Dotto periferico >4 cm con setti irregolari
Noduli parietali >1 cm
Interessamento multifocale
Ostruzione biliare

Gourgiotis S, Ridolfini MP, Germanos S. Intraductal papillary mucinous neoplasms of the pancreas.
EJSO 2007

MD Morgan. Cystic lesions of the pancreas. Seminars in Gastroenterology.
TUMORI SOLIDI

pancreas

papilla

Vie biliari
Tumore del pancreas

Sensibilità EUS 94%, sensibilità TAC 86%

Aumenta per lesioni < 3cm:
EUS 93%, TAC 53%, MRI 67%

Lesioni <2 cm:
EUS 90%, TAC 40%, MRI 33%

Accuratezza di EUS-FNA 85% - 95%

EUS permette di visualizzare lesioni non identificabili con altre metodiche.


Accuratezza N

Da valutare

perigastrici, periduodenali, del plesso celiaco, ilo epatico, mediastinici

Accuratezza EUS 64-82%, ma

NON DISTINGUE INFIAMMATORI/NEOPLASTICI

Invasione vascolare

Accuratezza EUS 40-100%, simile a MRI

**EUS/TAC**
- Infiltrazione venosa accuratezza simile
- Infiltrazione vena/arteria mesenterica, tripode celiaco
- TAC più accurata
- Infiltrazione della porta EUS più accurata
- Infiltrazione vena/arteria splenica più accurata EUS.

EUS ha una alta specificità (90%) ma sensibilità inferiore (73%) nel diagnosticare infiltrazione vascolare
Ca pancreatico e pancreatite cronica

Contrast-enhanced power Doppler (CEPD): ca pancreatico ipovascolare, tumori neuroendocrini e metastasi isovasculari o ipervasculari (aumento della sensibilità fino al 93%), pancreatite cronica non ha vascolarizzazione prime del contrasto, vascolarizzazione regolare dopo contrasto

Elastosonografia: tumori tessuti duri, quelli infiammatori “soft”

Per migliorare l’accuratezza:

Sensibilità EUS inferiore 75% specialmente nel caso di pancreatite cronica


Neoplasie del pancreas
3 passaggi con ago da 25 G: adk pancreatico
2 passaggi con ago da 25 G: adk pancreatico
TUMORI NEUROENDOCRINI

**Incidenza:**
aumento 300-500% negli ultimi 35 anni in USA

**Classificazione:**
secondo il neuropeptide predominante

Funzionanti o non funzionanti

**EUS**
Lesioni ipoecogene, a margini netti, ovoidali, ipervascolarizzati

Specificità
EUS 67%, PET 83%, TAC 80%

Accuratezza sovrapponibile

Confronto EUS e TAC in 34 pazienti:

**EUS** non ha identificato 1 tumore 15 mm

**TAC** non ha identificato 8 lesioni


Accuratezza EUS è

67% per T1, 71% per T2, 83% per T3


Accuratezza dell’EUS 84,4%


EUS più sensibile della spiral TAC per lesioni inferiori a 3 cm

(100% versus 56%)


EUS più accurata della TAC per tumori inferiori a 2 cm

(99% versus 70%)

Diagnosi

EUS
altamente sensibile nell’identificare tumori anche di piccole dimensioni, invasione vascolare superiore alla TAC, alla RMN, alla PET

Se disponibile, deve essere eseguita prima della rimozione endoscopica e/o chirurgia

ERCP permette:
eseguire biopsie, eseguire manovre operative.
ampulloma

Dilatazione del coledoco a monte
ERCP con biopsie/citologia è necessaria per avere istologia (20% stenosi benigno)

EUS utile per determinare la causa della stenosi (tumore testa pancreatica, pancreatite cronica) e per la valutazione linfonodale

EUS+FNA sensibilità: 43-86% per stenosi biliari
25-83% stenosi dell’ilo epatico

Calcolosi coledoco
Pancreatite cronica calcifica
Caratteristiche EUS di malignità

Componente solida associata alla cisti
- Vegetazioni parietali
- Cisti complesse
  - Dimensioni >2 cm
- Dilatazioni dotti pancreatici
- Linfoadenomeaglie

Accuratezza dell’EUS da sola varia 51-73%

EUS + FNA

N. Pausawasdi, JM Scheiman
Pancreatic cystic lesions. Curr Opin Gastroenterol 2010;26:506-12
EUS + FNA

Citologia
Ricerca cellule epiteliali colonnari → mucina (tumori mucoidi, tumori introduttali papillare mucinoso)
Ricerca cellule epiteliali cuboidali → glicogeno (tumori sierosi)

Chimica
Amilasi → elevate nelle pseudocisti, IPMN, tumori mucinosi
basse tumori sierosi
Lipasi → elevate (>6000 U/L) pseudocisti e IPMN
basse

Molecolare
KRAS, p53

EUS + FNA

Markers

CEA, CA 19-9, CA 125 CA72-4

CEA è il più accurato

- Elevato nelle forme mucinose
- Basso nelle forme sierose

(CEA < 5ng/mL sensibilità 50-100%
specificità 77-95% per sierosi)

(CEA > 192 ng/ml sensibilità 75%
specificità 84% per mucinosi)

(CEA > 800 ng/ml specificità 98%)