Καρκίνος παγκρέατος: Η θέση του γαστρεντερολόγου στο πλαίσιο της πολυεπιστημονικής ομάδας αντιμετώπισής του

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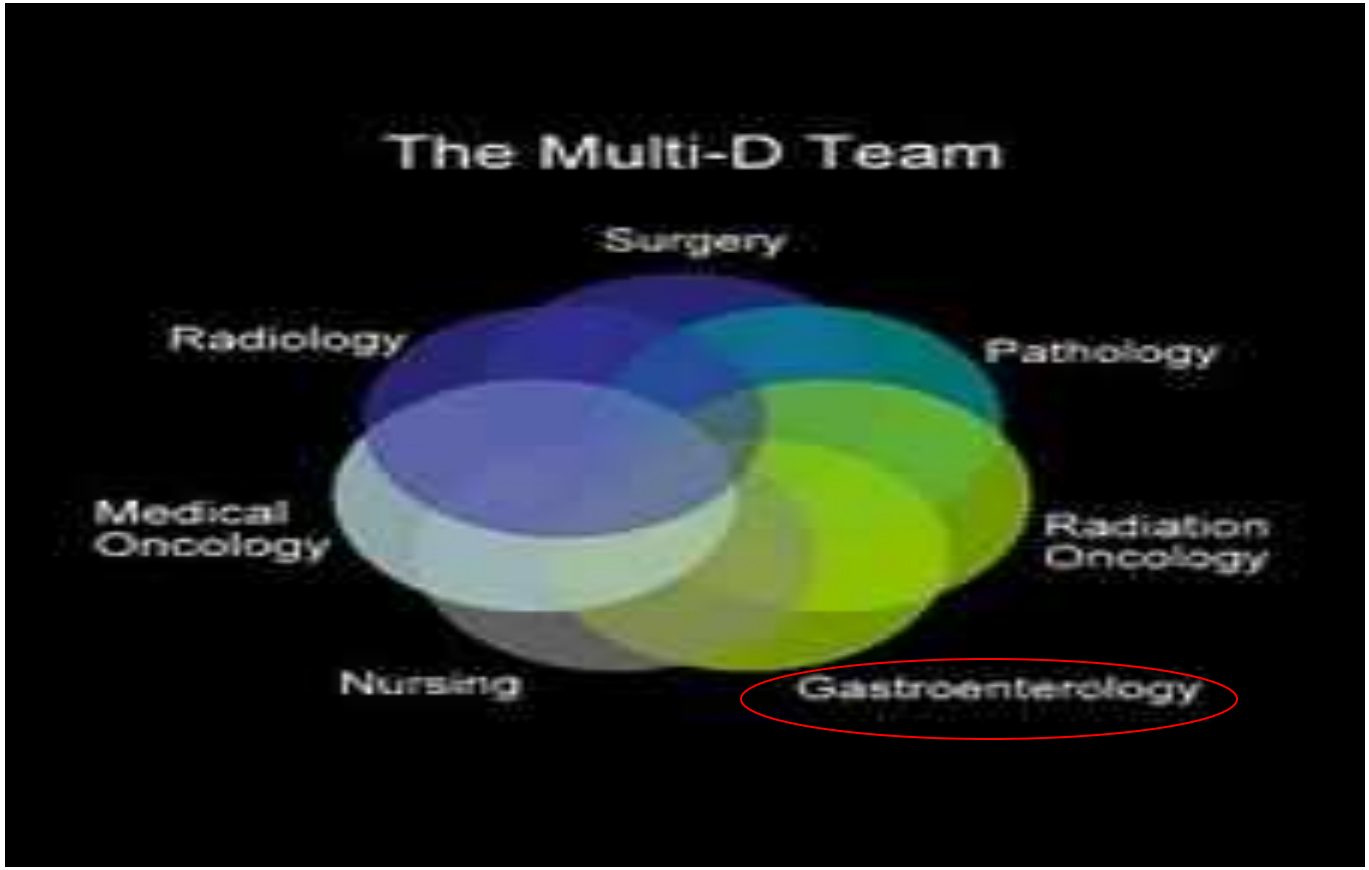
06.03.2020

Πολυεπιστημονική ομάδα (MDT) στον καρκίνο παγκρέατος



Ο Γαστρεντερολόγος στον καρκίνο του παγκρέατος

- Διαγνωστική προσέγγιση

- Σταδιοποίηση – αξιολόγηση εξαιρεσιμότητας

- Παρηγορητική αντιμετώπιση

- Ίκτερος
- Απόφραξη γαστρικής εξόδου
- Άλγος
- Ανεπάρκεια εξωκρινούς μοίρας

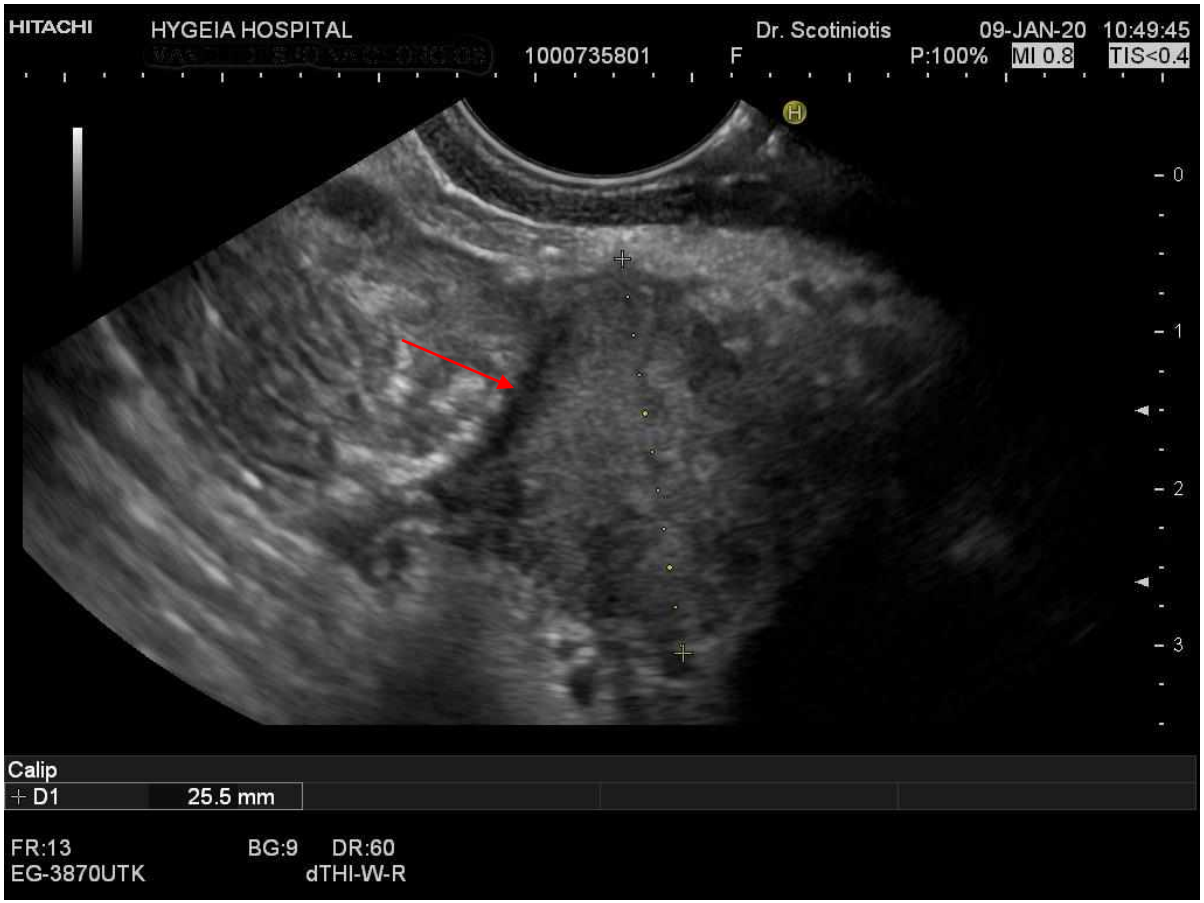
EUS: διαγνωστική προσέγγιση

- Ευαισθησία 93-95%
- Υπερτερεί σε σχέση με CT ή MRI σε όγκους <2 cm
- Ασθενείς με υποψία Ca παγκρέατος αλλά ασαφή ακτινολογικά ευρήματα → υψηλή αρνητική προγνωστική αξία (NPV)

Clin Gastroenterol & Hepatol 2006;4:717-25

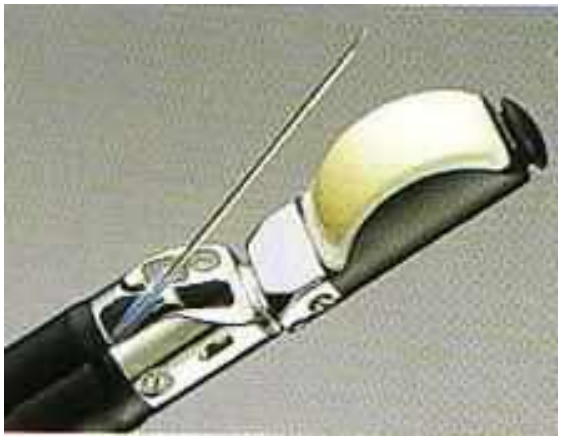
Gastrointest Endosc 2003;58:836-40

EUS: μάζα παγκρέατος



EUS - FNA

- Ευαισθησία: 89-92%, ειδικότητα: 96%
- On site Κυτταρολόγος ⟶ διαγνωστική ακρίβεια: 90-95%
- Τυχαιοποιημένη μελέτη ευαισθησίας με 84 ασθενείς:
  EUS-FNA: 84% vs. CT/US-FNA: 62% (P=0,074)



Pancreas. 2013;42:20-6
Gastrointest Endosc. 2000;51:184-90
Gastrointest Endosc. 2006;63:966-75

EUS - FNA

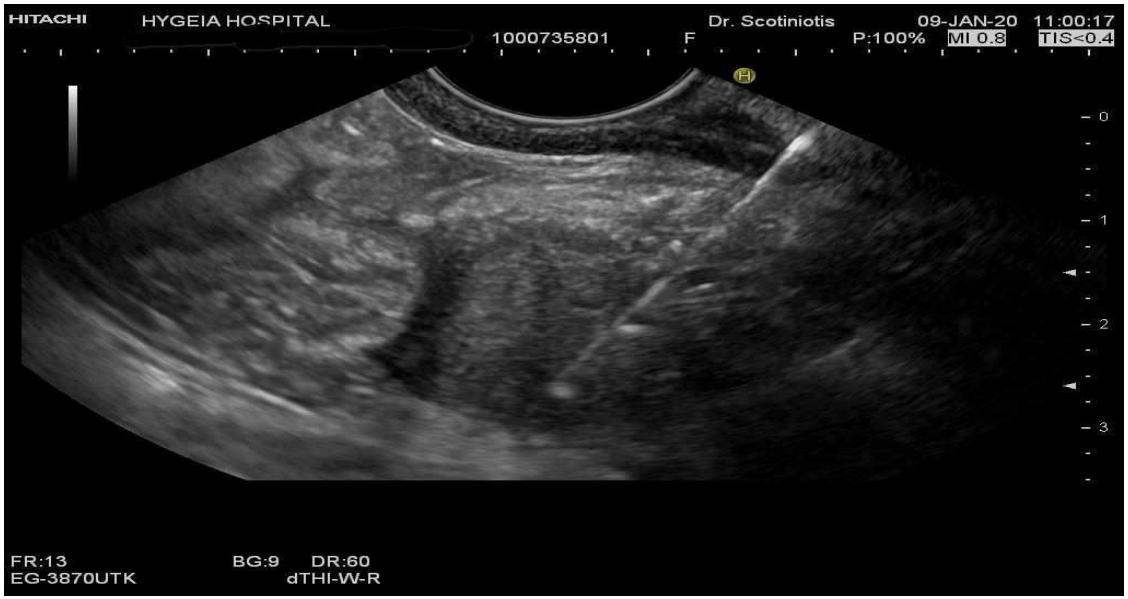
- Απαραίτητη για χορήγηση ΧΜΘ (neoadjuvant ή definitive)
- Υψηλότερη διαγνωστική απόδοση πριν την ERCP για τοποθέτηση SEMS
- Μη αναγκαία σε άμεσα εγχειρήσιμη νόσο
- Ασφαλής

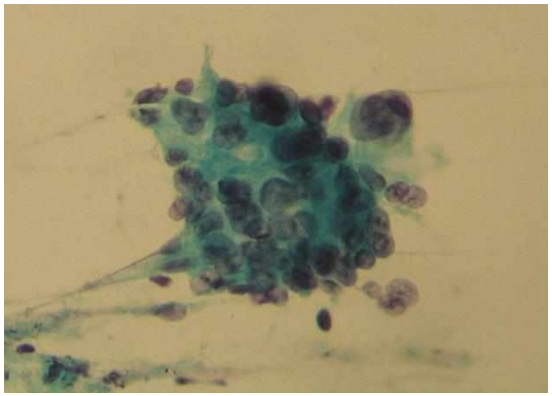
- παγκρεατίτιδα: 0,6%, αιμορραγία: 0,3%

- Needle tract seeding: 2,2% (CT-FNA: 16,3%)

Gastrointest Endosc 2013;77:839-43
Gastrointest Endosc 2003;58:690-95

EUS - FNA





ΑδενοCa

EUS: σταδιοποίηση / αξιολόγηση εξαιρεσιμότητας

- **Διήθηση αγγείων**
- Ευαισθησία: 66-86%
- Ειδικότητα: 89-94%

- **Επιχώριοι λεμφαδένες**
- Ευαισθησία: 69%
- Ειδικότητα: 81%

MDCT με παγκρεατικό πρωτόκολλο

JOP. 2013;14:484–97

Cancer Res Clin Oncol. 2014;140:2077–86

Σταδιοποίηση καρκίνου παγκρέατος

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Pancreatic Adenocarcinoma

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PRINCIPLES OF DIAGNOSIS, IMAGING, AND STAGING

- Decisions about diagnostic management and resectability should involve multidisciplinary consultation at a high-volume center with reference to appropriate high-quality imaging studies to evaluate the extent of disease. Resections should be done at institutions that perform a large number (at least 15–20) of pancreatic resections annually.

- High-quality dedicated imaging of the pancreas should be performed at presentation (even if standard CT imaging is already available), preferably within 4 weeks of surgery, and following neoadjuvant treatment to provide adequate staging and assessment of resectability status. Imaging should be done prior to stenting, when possible.

- Imaging should include dedicated pancreatic CT of abdomen (preferred) or MRI with contrast.
  - Multi-detector computed tomography (MDCT) angiography, performed by acquiring thin, preferably sub-millimeter, axial sections using a dual-phase pancreatic protocol, with images obtained in the pancreatic and portal venous phase of contrast enhancement, is the preferred imaging tool for dedicated pancreatic imaging.[a] Scan coverage can be extended to cover the chest and pelvis for complete staging as per institutional preferences. Multiplanar reconstruction is preferred as it allows precise visualization of the relationship of the primary tumor to the mesenteric vasculature as well as detection of subcentimeter metastatic deposits. See MDCT Pancreatic Adenocarcinoma Protocol, PANC-A (3 of 8).
  - MRI is most commonly used as a problem-solving tool, particularly for characterization of CT-indeterminate liver lesions and when suspected pancreatic tumors are not visible on CT or when contrast-enhanced CT cannot be obtained (as in cases with severe allergy to iodinated intravenous contrast material). This preference for using MDCT as the main imaging tool in many hospitals and imaging centers is mainly due to the higher cost and lack of widespread availability of MRI compared to CT. See MRI Pancreatic Adenocarcinoma Protocol, PANC-A (4 of 8).

- The decision regarding resectability status should be made by consensus at multidisciplinary meetings/discussions following the acquisition of dedicated pancreatic imaging including complete staging. Use of a radiology staging reporting template is preferred to ensure complete assessment and reporting of all imaging criteria essential for optimal staging, which will improve the decision-making process.[a] See Pancreatic Cancer Radiology Reporting Template, PANC-A (5 of 8).

Σταδιοποίηση καρκίνου παγκρέατος

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PRINCIPLES OF DIAGNOSIS, IMAGING, AND STAGING

- The role of PET/CT (without iodinated intravenous contrast) remains unclear. Diagnostic CT or MRI with IV contrast as discussed above in conjunction with functional PET imaging can be used per institutional preference. PET/CT scan may be considered after formal pancreatic CT protocol in high-risk[b] patients to detect extra pancreatic metastases. It is not a substitute for high-quality, contrast-enhanced CT.
- EUS is not recommended as a routine staging tool. In select cases, EUS may be complementary to CT for staging.
- EUS-FNA/fine-needle biopsy (FNB) is preferable to a CT-guided FNA in patients with resectable disease because of better diagnostic yield, safety, and potentially lower risk of peritoneal seeding with EUS-FNA/FNB when compared with the percutaneous approach. Biopsy proof of malignancy is not required before surgical resection, and a non-diagnostic biopsy should not delay surgical resection when the clinical suspicion for pancreatic cancer is high.
- Diagnostic staging laparoscopy to rule out metastases not detected on imaging (especially for body and tail lesions) is used in some institutions prior to surgery or chemoradiation, or selectively in patients who are at higher risk[b] for disseminated disease. Intraoperative ultrasound can be used as a diagnostic adjunct during staging laparoscopy.
- Positive cytology from washings obtained at laparoscopy or laparotomy is equivalent to M1 disease. If resection has been done for such a patient, he or she should be treated for M1 disease.
- For locally advanced/metastatic disease, the panel recommends serial CT with contrast (routine single portal venous phase or dedicated pancreatic protocol if surgery is still contemplated) or MRI with contrast of known sites of disease to determine therapeutic benefit. However, it is recognized that patients can demonstrate progressive disease clinically without objective radiologic evidence of disease progression.
- Recent retrospective studies suggest that imaging characteristics may not be a reliable indicator of resectability in borderline resectable and locally advanced patients who have received neoadjuvant therapy. Determinations of resectability and surgical therapy should be made on an individualized basis in a multidisciplinary setting. (See Discussion for references)

Κριτήρια εξαιρεσιμότητας καρκίνου παγκρέατος

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Pancreatic Adenocarcinoma

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CRITERIA DEFINING RESECTABILITY STATUS[a]

Resectability Status	Arterial	Venous
Resectable	No arterial tumor contact (celiac axis [CA], superior mesenteric artery [SMA], or common hepatic artery [CHA]).	No tumor contact with the superior mesenteric vein (SMV) or portal vein (PV) or ≤180° contact without vein contour irregularity.
Borderline Resectable[b]	Pancreatic head/uncinate process: • Solid tumor contact with CHA without extension to CA or hepatic artery bifurcation allowing for safe and complete resection and reconstruction. • Solid tumor contact with the SMA of ≤180° • Solid tumor contact with variant arterial anatomy (ex: accessory right hepatic artery, replaced right hepatic artery, replaced CHA, and the origin of replaced or accessory artery) and the presence and degree of tumor contact should be noted if present, as it may affect surgical planning. Pancreatic body/tail: • Solid tumor contact with the CA of ≤180° • Solid tumor contact with the CA of >180° without involvement of the aorta and with intact and uninvolved gastroduodenal artery thereby permitting a modified Appleby procedure [some panel members prefer these criteria to be in the unresectable category].	• Solid tumor contact with the SMV or PV of >180°, contact of ≤180° with contour irregularity of the vein or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing for safe and complete resection and vein reconstruction. • Solid tumor contact with the inferior vena cava (IVC).
Unresectable[b]	• Distant metastasis (including non-regional lymph node metastasis) Head/uncinate process: • Solid tumor contact with SMA >180° • Solid tumor contact with the CA >180° Body and tail: • Solid tumor contact of >180° with the SMA or CA • Solid tumor contact with the CA and aortic involvement	Head/uncinate process: • Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus) • Contact with most proximal draining jejunal branch into SMV Body and tail: • Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus)

[a]Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology 2014 Jan; 270(1):248-260.
[b]Solid tumor contact may be replaced with increased hazy density/stranding of the fat surrounding the peri-pancreatic vessels (typically seen following neoadjuvant therapy); this finding should be reported on the staging and follow-up scans. Decision on resectability status should be made in these patients, in consensus at multidisciplinary meetings/discussions.

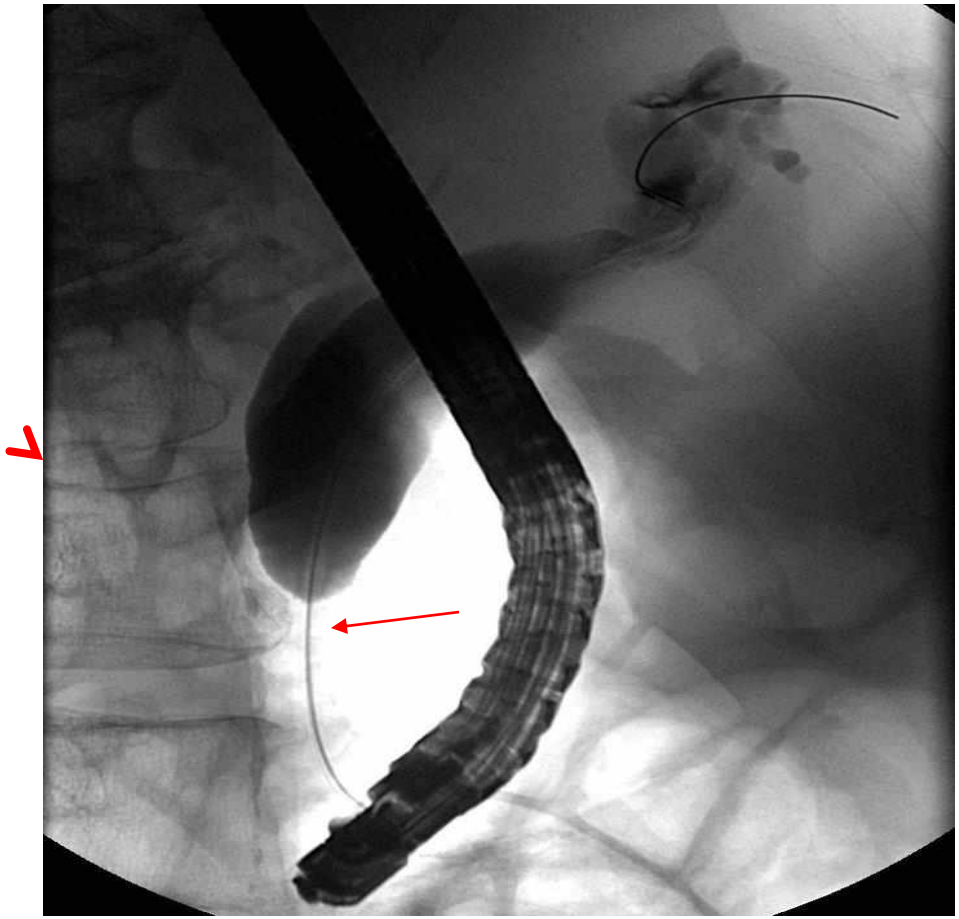
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Παρηγορητική αντιμετώπιση

- Ίκτερος
- Απόφραξη γαστρικής εξόδου
- Άλγος
- Ανεπάρκεια εξωκρινούς μοίρας

pancreaticcanceraction.org

ERCP: παροχέτευση χοληφόρων



ERCP: ποιο το σωστό timing;

Μη αναγκαία σε ασθενείς με άμεσα εγχειρήσιμη νόσο

RECOMMENDATION

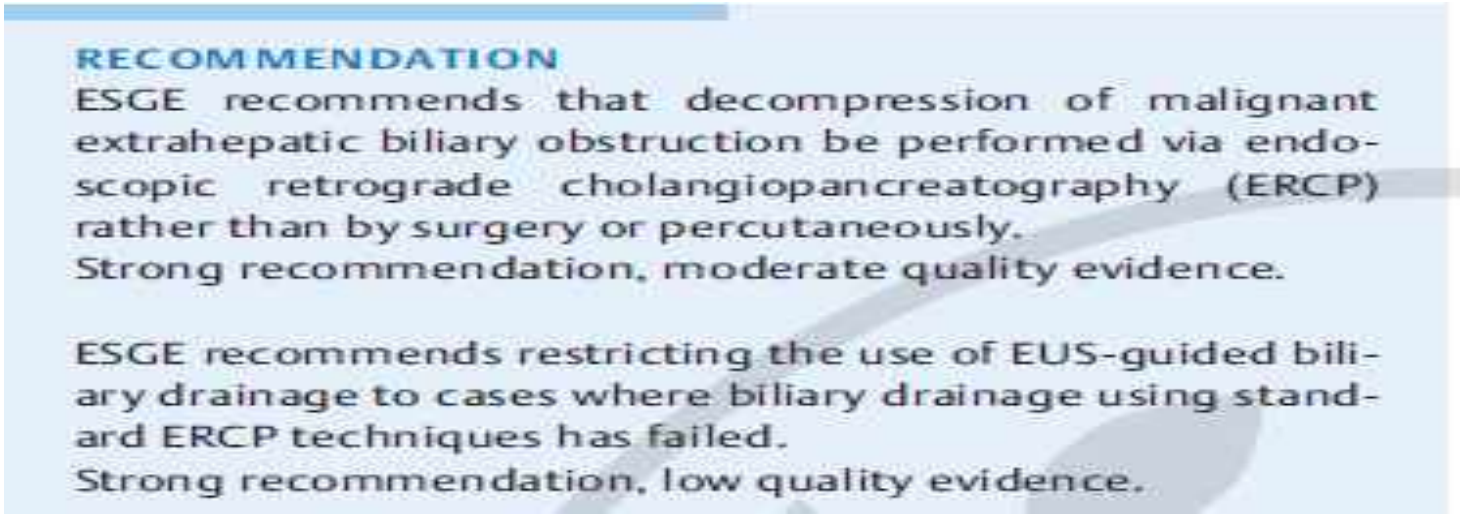
ESGE recommends against routine preoperative biliary drainage in patients with malignant extrahepatic biliary obstruction; preoperative biliary drainage should be reserved for patients with cholangitis, severe symptomatic jaundice (e.g., intense pruritus), or delayed surgery, or for before neoadjuvant chemotherapy in jaundiced patients.

Strong recommendation, moderate quality evidence.

ESGE 2017

ERCP vs. PTCD / χειρουργείο

ERCP: Λιγότερες επιπλοκές, μικρότερη νοσηρότητα, ταχύτερη ανάρρωση, μικρότερο κόστος



RECOMMENDATION

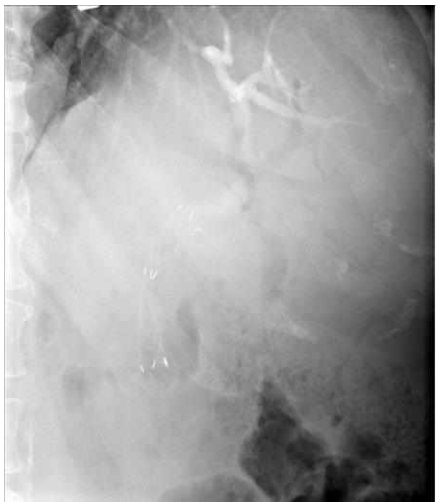
ESGE recommends that decompression of malignant extrahepatic biliary obstruction be performed via endoscopic retrograde cholangiopancreatography (ERCP) rather than by surgery or percutaneously.
Strong recommendation, moderate quality evidence.

ESGE recommends restricting the use of EUS-guided biliary drainage to cases where biliary drainage using standard ERCP techniques has failed.
Strong recommendation, low quality evidence.

ESGE 2017

ERCP: τύπος ενδοπρόθεσης

SEMS: Μεγαλύτερη διάρκεια βατότητας, λιγότερες καθυστερήσεις στην ΧΜΘ, παρόμοιο συνολικό κόστος, επιτρέπουν R0 εκτομή, δεν αυξάνουν περιεγχειρητική νοσηρότητα / θνητότητα



RECOMMENDATION

ESGE recommends the endoscopic placement of a 10-mm diameter self-expandable metal stent (SEMS) for pre-operative biliary drainage of extrahepatic malignant biliary obstruction.

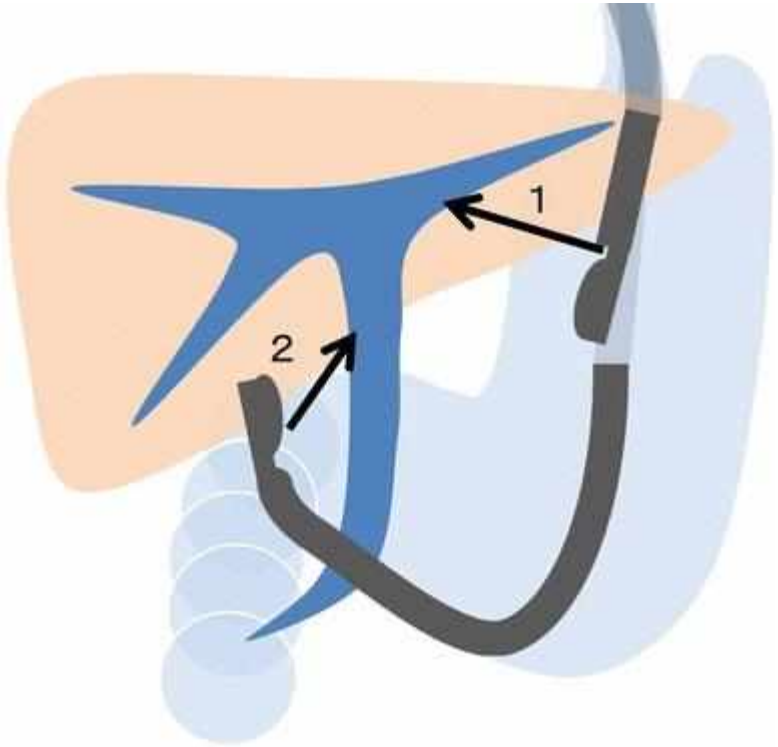
Strong recommendation, moderate quality evidence.

ESGE 2017

EUS-κατευθυνόμενη παροχέτευση χοληφόρων (EUS-BD)

- Επί τεχνικά αδύνατης ή αποτυχημένης ERCP
- «χολοπεπτική» αναστόμωση (διαγαστρική ή διαδωδεκαδακτυλική) με τοποθέτηση stent
- Τεχνική randezvous

1. ηπατικογαστρική αναστόμωση (HGS)
2. χοληδοχοδωδεκαδακτυλική αναστόμωση (CDS)



Τεχνική randezvous

EUS-BD vs. ERCP (ως πρώτης γραμμής μέθοδοι)

- Παρόμοια τεχνική επιτυχία
- Παρόμοια κλινική επιτυχία
- Παρόμοια ασφάλεια
- Απαιτεί υψηλή εξειδίκευση

Sci Rep 2019;9:16551
Dig Endosc 2020;32:16-26

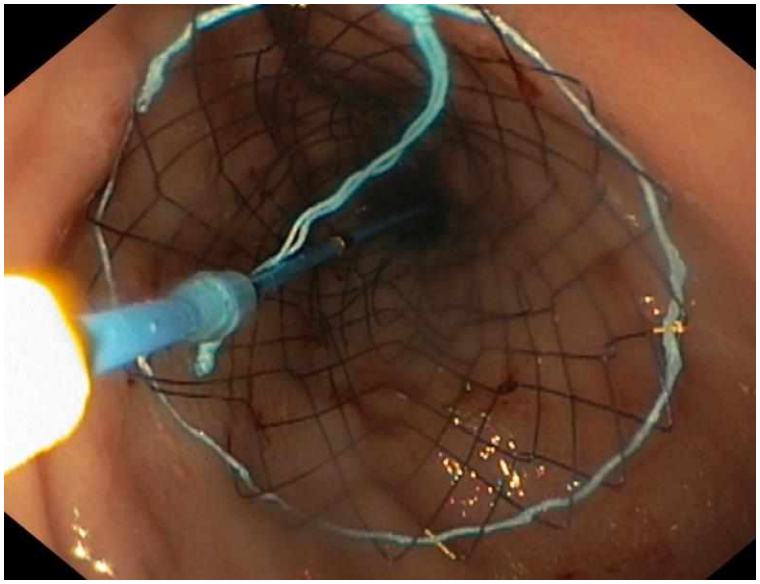
Απόφραξη γαστρικής εξόδου

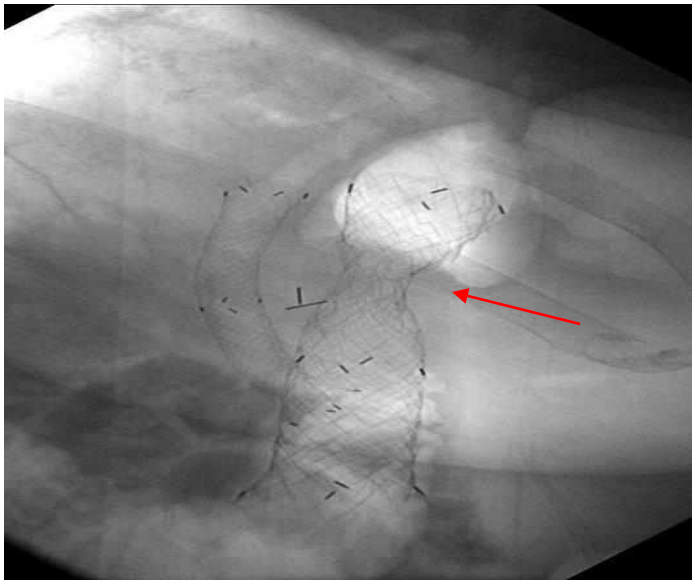
- 10-25% των ασθενών

- SEMS vs. γαστρεντεροαναστόμωση
  - Λιγότερες επιπλοκές
  - Ταχύτερη per os σίτιση
  - Μικρότερη νοσηλεία
  - Μικρότερο κόστος
  - Παρόμοια επιβίωση / ποιότητα ζωής

J Gastrointest Oncol. 2014;5:92–8
Gastrointest Endosc. 2010;71:490–9

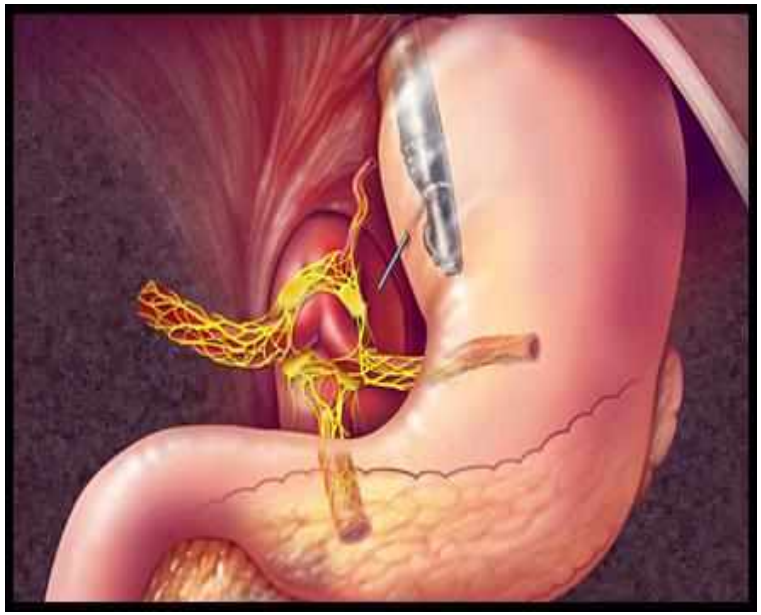
Απόφραξη γαστρικής εξόδου





Αντιμετώπιση άλγους

- EUS - κατευθυνόμενη νευρόλυση κοιλιακού πλέγματος
- Bupivacaine + ETOH (98%)
- Βελτίωση στο 70-85% των ασθενών



Dig Dis Sci. 2009;54:2330-7

Ανεπάρκεια εξωκρινούς μοίρας

- 64-100% των ασθενών
- Πολυπαραγοντικής αιτιολογίας
- Υποκατάσταση παγκρεατικών ενζύμων (PERT)
- Διατροφικές τροποποιήσεις
  - Μικρά και συχνά γεύματα
  - Μη αναγκαίος ο περιορισμός του λίπους

J Gastroenterol Hepatol. 2011;26 Suppl 2:12

Screening στον παγκρεατικό καρκίνο;

- Αναγνώριση μελών της οικογενείας σε αυξημένο κίνδυνο (οικογενής προδιάθεση ή γενετικά σύνδρομα)
- Εξατομικευμένο screening / surveillance
- MRI/MRCP, EUS
- Στόχοι: T1N0M0, PanIN / IPMN με HGD

Gut 2020;69:7-17

Screening στον παγκρεατικό καρκίνο;

Table 3 Summary of the main recommendations of the 2019 International Cancer of the Pancreas Surveillance (CAPS) Consortium

Who?		
► All patients with Peutz-Jeghers syndrome (carriers of a germline *LKB1/STK11* gene mutation) ► All carriers of a germline *CDKN2A* mutation ► Carriers of a germline *BRCA2*, *BRCA1*, *PALB2*, *ATM*, *MLH1*, *MSH2*, or *MSH6* gene mutation with at least one affected first-degree blood relative ► Individuals who have at least one first-degree relative with pancreatic cancer who in turn also has a first-degree relative with pancreatic cancer (familial pancreatic cancer kindred)		
When (at what age)?		
► Age to initiate surveillance depends on an individual's gene mutation status and family history		
Familial pancreatic cancer kindred (without a known germline mutation)		Start at age 50 or 55* or 10 years younger than the youngest affected blood relative
Mutation carriers: For *CDKN2A*†, Peutz-Jegher syndrome, start at age 40; *BRCA2,ATM, PALB2 BRCA1, MLH1/MSH2* start at age 45 or 50 or 10 years younger than youngest affected blood relative		
► There is no consensus on the age to end surveillance		
How?		
At baseline	► MRI/MRCP+EUS + fasting blood glucose and/or HbA1c	
During follow-up	► Alternate MRI/MRCP and EUS (no consensus if and how to alternate) ► Routinely test fasting blood glucose and/or HbA1c	
On indication	► Serum CA 19–9	► If concerning features on imaging
	► EUS-FNA only for	► Solid lesions of ≥5 mm ► Cystic lesions with worrisome features ► Asymptomatic MPD strictures (with or without mass)
	► CT only for	► Solid lesions, regardless of size ► Asymptomatic MPD strictures of unknown aetiology (without mass)
Intervals and surgery		
12 Months	► If no abnormalities, or only non-concerning abnormalities (eg, pancreatic cysts without worrisome features)	
3 or 6 Months	► If concerning abnormalities for which immediate surgery is not indicated (see figure 2 for details)	
Surgery	► If positive FNA and/or a high suspicion of malignancy on imaging (see figure 2 for details)	
► When surgery is indicated, perform an oncological radical resection at a specialty centre		
Goals		
The goal of surveillance is to detect and treat the following pathological lesions		► Stage I pancreatic cancer, confined to the pancreas, resected with negative margins ► Pancreatic cancer precursor lesions with high-grade dysplasia (PanIN or IPMN)

Συμπεράσματα 1

- Ανίχνευση μικρών βλαβών επί κλινικής / απεικονιστικής υποψίας (EUS)
- Τοπική σταδιοποίηση με EUS μόνο συμπληρωματικά της MDCT σε επιλεγμένες περιπτώσεις
- Λήψη υλικού (EUS-FNA) πριν την ΧΜΘ (neoadjuvant, definitive)
- EUS-FNA πριν την ERCP

Συμπεράσματα 2

- Παροχέτευση χοληφόρων με SEMS (ERCP)
- Αντιμετώπιση απόφραξης γαστρικής εξόδου (SEMS)
- Αντιμετώπιση καρκινικού πόνου (EUS-CPN)
- Διατροφική καθοδήγηση / PERT
- Αναγνώριση ατόμων υψηλού κινδύνου προς screening/surveillance

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