ENDOSCOPIC ULTRASOUND (EUS) AND PANCREATIC CANCER

SEPTEMBER 2024

EDUARDO CHUA MD

DISCLOSURES

- No relevant financial disclosures

2

OBJECTIVES

- Provide a brief overview of endoscopic ultrasound and clinical uses
- Provide a brief overview of pancreatic cancer
- Describe the role of EUS In the investigation of pancreatic cancer

3

WHAT IS EUS?

- Convergence of ultrasound and endoscopy
- ultrasound probe at scope tip allows detailed views of GI tract wall and adjacent structures
- History: first published reports in 1980s, increasing clinical use since 1990s

4

EUS ALLOWS US TO SEE...

- Esophagus: esophageal wall, mediastinal structures (aorta, heart, azygous vein, right/left pleura, mediastinal LN, etc.)
- Stomach: gastric wall, pancreas (body/tail), celiac vessels, liver, GB, spleen, left adrenal, left kidney
- Duodenum: duodenal wall, ampulla, pancreas (head/uncinate), CBD, GB, portal vein, right kidney
- Rectum: rectal wall, anal sphincter, perirectal structures (prostate, uterus), iliac vessels

5

EUS: MAINSTREAM CLINICAL USES

- ***Evaluation of GI luminal tract disease:***
  - GI cancers: esophageal, gastric, rectal
  - GI wall subepithelial lesions
- ***Evaluation of pancreatico-biliary disease:***
  - Known or suspected pancreatic cancer
  - Pancreatic cysts
  - Biliary stones
  - Acute and chronic pancreatitis
  - Lymph node assessment

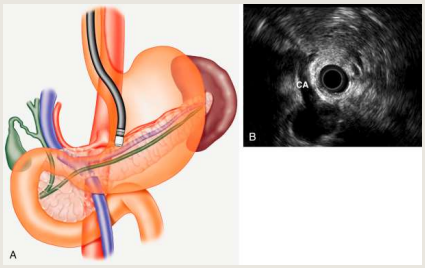
6

EUS: MAINSTREAM CLINICAL USES

- ***Therapeutic interventions***
  - Stent placement (LAMS)
    - Drainage of fluid collections (cystgastrostomy)
    - Intestinal Bypass (gastrojejunostomy)
    - Bridge to surgery in sicker patients (i.e choleduodenostomy)
  - Fiducial placement
  - Celiac plexus neurolysis

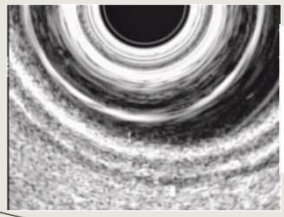
7

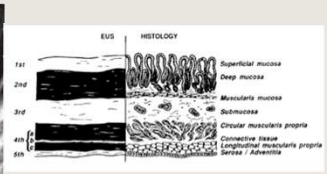
RADIAL IMAGING



8

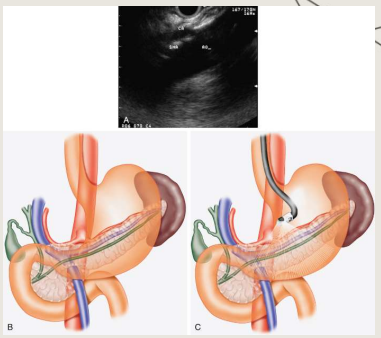
EUS : NORMAL GI TRACT WALL





9

LINEAR IMAGING



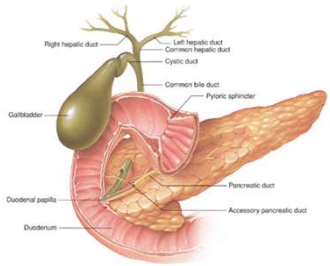
10

EUS FINE NEEDLE ASPIRATION/BIOPSY

	EUS-FNA	EUS-FNB						
		1st-Gen	2nd-Gen	3rd-Gen				
Needle tip	Menghini	Tru-cut	Reverse bevel	Fork-tip	Franseen	Forward bevel	Franseen	Fork-tip
Available Sizes	19-25G	19G	19, 22, 25G	19, 22, 25G	22, 25G	20G	19, 22, 25G	19, 22, 25G
Commercial name	Many	Quick-Core	ProCore	SharkCore	Acquire	Procore	TopGain	EZ Shot
Corporation	Many	Cook Endoscopy	Cook Endoscopy	Medtronic	Boston Scientific	Cook Endoscopy	Medi-Globe	Olympus

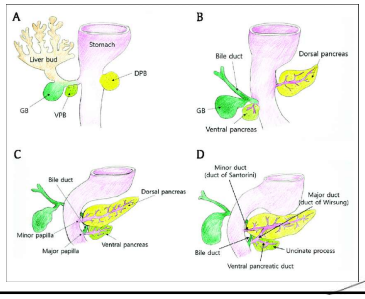
11

PANCREATIC CANCER



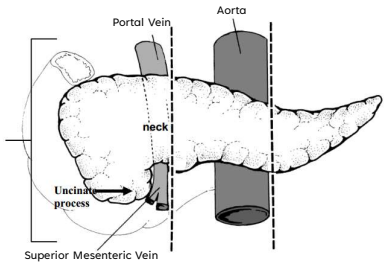
12

DEVELOPMENT OF THE PANCREAS



13

PARTS OF THE PANCREAS



Head **Body** **Tail**

PANCREATIC CANCER

- Lifetime Risk of Developing Cancer: Approximately 1.7 percent of men and women will be diagnosed with pancreatic cancer at some point during their lifetime, based on 2018–2021 data
- Prevalence of This Cancer: In 2021, there were an estimated 100,669 people living with pancreatic cancer in the United States.
- new pancreatic cancer cases have been rising on average 0.9% each year over 2012–2021

from National Cancer Institute, SEER data

15

PANCREATIC CANCER

- Estimated New Cases in 2024 66,440
  - % of All New Cancer Cases 3.3%
- Estimated Deaths in 2024 51,750
  - % of All Cancer Deaths 8.5%
- 5-Year Relative Survival (2014-2020) 12.8%

from National Cancer Institute, SEER data

16

RISK FACTORS FOR PANCREATIC CANCER

- Modifiable
  - Smoking
  - Obesity
  - Personal history of diabetes
  - Personal history or chronic pancreatitis

17

RISK FACTORS FOR PANCREATIC CANCER

- Nonmodifiable
  - Age (67% of cases in patients 65 and above)
  - Race (increased risk in African Americans)
  - Family history of pancreatic cancer

18

RISK FACTORS FOR PANCREATIC CANCER

- Nonmodifiable
  - Inherited genetic mutations
    - Hereditary breast and ovarian cancer syndrome (HBOC), caused by mutations in the BRCA1 or BRCA2 genes
    - Hereditary breast cancer, caused by mutations in the PALB2 gene
    - Ataxia telangiectasia (AT), caused by mutations in the ATM gene
    - Familial atypical multiple mole melanoma (FAMMM) syndrome, caused by mutations in the p16/CDKN2A gene and associated with skin and eye melanomas
    - Hereditary pancreatitis, usually caused by mutations in the PRSS1 gene
    - Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), most often caused by a defect in the MLH1 or MSH2 genes
    - Peutz-Jeghers syndrome, caused by defects in the STK11 gene. This syndrome is also linked with polyps in the digestive tract and several other cancers.

19

SYMPTOMS OF PANCREATIC CANCER

- Asthenia (weakness) – 86 percent
- Weight loss – 85 percent
- Anorexia (no appetite)– 83 percent
- Abdominal pain – 79 percent
- Epigastric pain (stomach) – 71 percent
- Dark urine – 59 percent
- Jaundice – 56 percent
- Nausea – 51 percent
- Back pain – 49 percent
- Diarrhea- 44 percent
- Vomiting – 33 percent
- Steatorrhea (fatty stools)– 25 percent
- Thrombophlebitis – 3 percent

20

SIGNS OF PANCREAS CANCER

- Jaundice – 55 percent
- Hepatomegaly (liver enlargement) - 39 percent
- Right upper quadrant mass – 15 percent
- Cachexia (wasting) – 13 percent
- Courvoisier's sign (nontender but palpable distended gallbladder at the right costal margin) – 13 percent
- Epigastric mass (palpable lump in stomach) – 9 percent
- Ascites (abdominal fluid) – 5 percent

21

DIFFERENTIAL DIAGNOSIS

- Chronic pancreatitis
- Benign Neuroendocrine tumors (NET)
- Autoimmune pancreatitis (especially in younger patients)
- Lymphoma
- Metastatic tumor (renal, colon, melanoma, breast, lung)

22

TYPES OF PANCREATIC CANCER

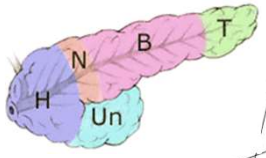
- Exocrine carcinoma: Over 90% of all pancreatic tumors are exocrine tumors. The most common type of pancreatic cancer is adenocarcinoma.
- Neuroendocrine carcinoma: Less than 10% of pancreatic tumors are neuroendocrine tumors (NETs). Islet cell carcinoma is another name for a NE cancer.

23

LOCATION OF PANCREAS CANCER

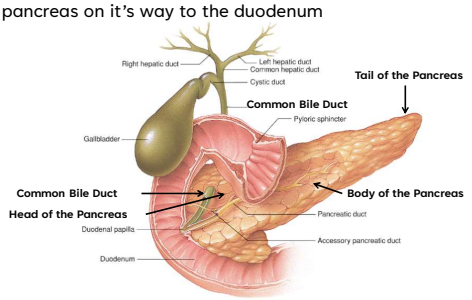
- 60 to 70 percent of exocrine pancreatic cancers are localized to the head
- 20 to 25 percent are in the body/tail and
- the remainder involve the whole organ

H = Head
N = Neck
B = Body
T = Tail
Un = Uncinate

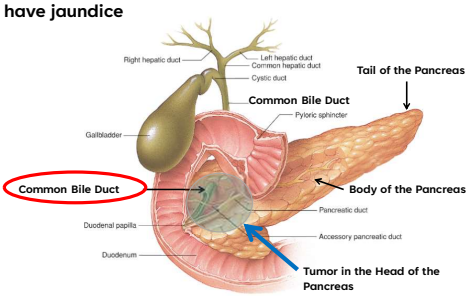


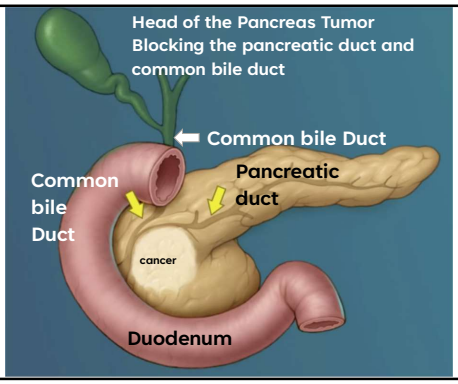
24

Bile duct carries the bile through the head of the pancreas on it's way to the duodenum

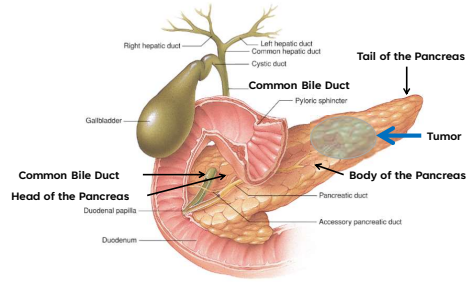


Tumors in the head of the pancreas are more likely to have jaundice





Tumors in the body or tail are more likely to present with pain or weight loss



TESTS USED TO EVALUATE AND STAGE PANCREAS CANCER

- Routine blood tests e.g. liver function tests like bilirubin
- Elevated tumor markers (CA 19-9 or CEA)
- MRI, CT scans, Ultrasound
- Endoscopic ultrasound or ERCP
- Laparoscopy

29

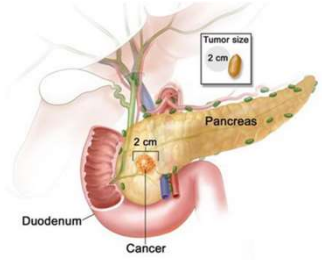
TNM STAGING

- T (tumor size/extent)
- N (nodal involvement)
- M (metastasis)

- combine all 3 to get Stage

30

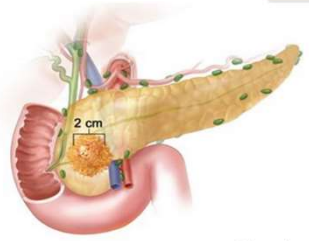
STAGE IA (T1N0M0)



31

STAGE IB (T2N0M0)

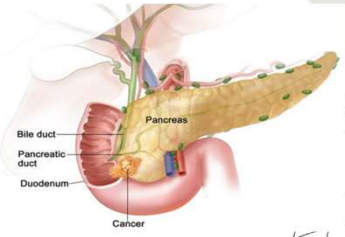
over 2cm, limited to pancreas



32

STAGE IIA (T3N0)

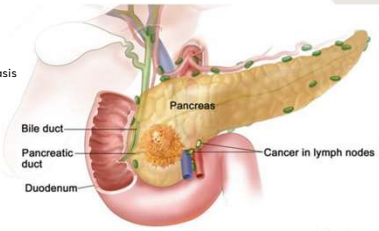
Tumor extending beyond the pancreas with out involvement of the celiac artery or superior mesenteric artery



33

STAGE IIB (T1-3N1M0)

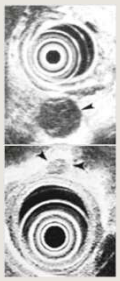
Regional lymph node metastasis



34

EUS: LYMPH NODE ASSESSMENT

- Malignant characteristics:
  - size > 1cm
  - homogeneous, hypoechoic pattern
  - round
  - smooth borders
- *High accuracy (>80%) when all 4 features present --* *Catalano MF. GIE 1994; 40:442*



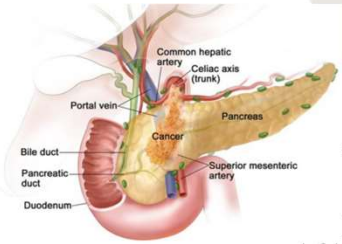
malignant

benign

35

STAGE III (T4) UNRESECTABLE

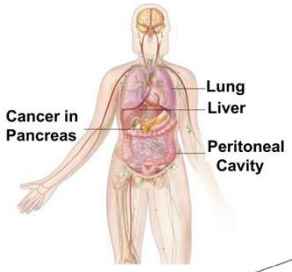
Cancer has spread to the major blood vessels near the pancreas. These include the superior mesenteric artery, celiac axis



36

STAGE IV (ANY T, ANY N, M1)

Cancer has spread to distant organs or to the peritoneal cavity



37

NCDB STATISTICS

Stage	Incidence	Survival/5y
I	8.5%	20%
II	23%	10%
III	14%	2.5%
IV	54%	1.6%

38

CASE

- 60 year-old male presents with a 30 lb. unintentional wt loss over 4 months, and 2 week history of jaundice. He denies abdominal pain or fevers. TBili=12, DBili=8, Alk Phos=650.
- An MRI/MRCP was obtained- marked CBD dilation with "fullness" of the pancreatic head, no definite mass. The patient has done research on the internet, and asks if the next step is ERCP ?

39

CASE

- *Did the MRI miss a tumor? How often does that occur?*
- *What is the role of EUS?*
- *What is the role of ERCP in suspected pancreatic CA?*

40

BEST TEST TO DETECT PANCREATIC CANCER? SENSITIVITY OF CT/MRI VS. EUS

study	N	MRI	CT	EUS	p significant
Palazzo 1993	64		69%	96%	+
Yasuda 1993	29		72%	100%	+
Muller 1994	49	83%	69%	94%	+ (EUS vs CT)
Nakaizumi 1995	232		65%	94%	+
Sugiyama 1997	73		81%	96%	+
Gress 1999	81		74%	100%	+
Mertz 2000	35		53%	93%	+
DeWitt 2004	80		86%	98%	+
Borbath 2005	59	88%		98%	ns

41

DETECTION OF SMALL TUMORS (< 2.5 - 3CM)

study	N	sensitivity: CT	EUS
Palazzo 1993	7	14%	100%
Muller 1994	15	53%	93%
DeWitt 2004	19	53% (MDCT)	89%

Main benefit of EUS over CT is detection of small lesions

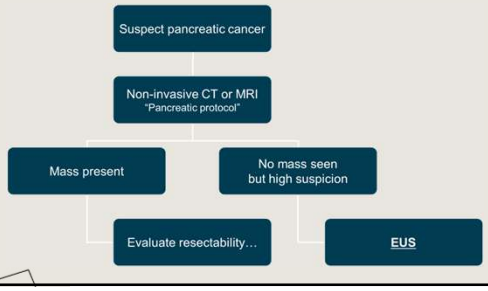
42

WHERE DOES PET FIT INTO TUMOR DETECTION?

study	N	sensitivity: PET	CT or MRI	EUS
Mertz 2000	35	87%	53%	93%
Lytras 2005	112	73%	89%	
Borbath 2005	59	88%	88%	98%

43

ALGORITHM FOR PANCREATIC TUMOR DETECTION



44

SO WHAT IF EUS IS *"NORMAL"* IN A PATIENT WITH SUSPECTED PANCREATIC CANCER ON IMAGING?

study	N	follow-up	results
Chak 2003	58 / 80	minimum - 6 mo mean - 24 mo	*no cancer*
Chang 2005	155 / 693	8 - 48 mo mean - 24 mo	*no cancer*
Gress 2006	21 / 50	median - 27 mo	*no cancer*

45

MAIN CLINICAL QUESTIONS AFTER DETECTION OF PANCREATIC CANCER

- Does the mass appear surgically resectable?
  - What is the best test to determine resectability?
- Is a tissue diagnosis needed?
  - Best method to collect tissue sample?
  - CT-bx? ERCP with brushings? EUS-FNA?

46

ACCURACY IN ASSESSING RESECTABILITY IN PANCREATIC CANCER

study	N	MRI	CT	EUS	p-value
Gress 1999	81		60%	93%	<0.001
Ahmad 2000	63	77%		69%	ns
Ramsay 2004	27	83%	76%	63%	ns
Soriano 2004	62	75%	83%	67%	ns
DeWitt 2004	53		77%	77%	ns

CT/MRI + EUS may be more accurate than either alone

Ahmad 2000, Soriano 2004

47

CASE CONTINUED...

EUS reveals a 3 cm mass in the pancreas that abuts the portal vein - potentially resectable. He is referred to surgery. The patient has history of CAD. The surgeon and patient are reluctant to proceed with a Whipple operation unless a diagnosis of cancer is confirmed. How should this mass be biopsied?

(1) CT guided bx

(2) ERCP

(3) EUS-FNA

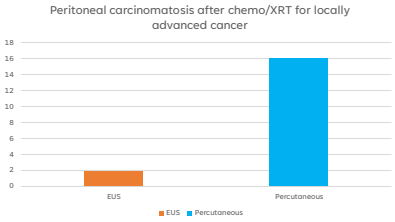
48

BEST METHOD FOR PANCREATIC TUMOR BIOPSY? EUS-FNA VS. CT/US-FNA

- *Horwhat GIE 2006*: Single-center, randomized prospective cross-over study (1997-2002)
  - EUS-FNA (n=41) CT/US (n=43)
- Sensitivity for diagnosing pancreatic cancer higher with EUS:
  - EUS-FNA: 84%
  - CT / US guided FNA: 62% (p=0.12)
- Unable to reach target enrollment (attributed to increased referral specifically for EUS-FNA)

49

COMPLICATIONS OF TISSUE SAMPLING (FNA/FNB) EUS VS. PERCUTANEOUS



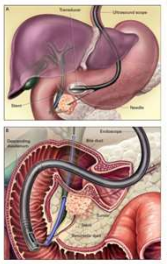
2% vs. 16% ; p=0.025

Micames GIE 2003

50

TISSUE SAMPLING IN PANCREATIC CANCER EUS-FNA OR ERCP?

	sensitivity	Procedure related pancreatitis
EUS-FNA	>85%	1-2%
ERCP	40-75%	3-5%



Fritscher-Ravens, AJG 2000
Kochman, JCO 1997
Jacobsen, GIE 2005
Jaiwals, GIE 2000
Brugge, GIE 2010

51

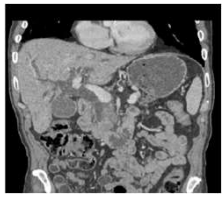
WHAT IS THE ROLE OF ERCP IN PANCREATIC CANCER?

- Tumor detection: ***No role***
  - ERCP can show dilated ducts
  - CT/MRI/EUS more sensitive and less risky (cholangitis, pancreatitis)
- Tumor staging: ***No role***
  - Extent of bile / pancreatic duct involvement rarely relevant for consideration of resectability
  - Similar info readily available on CT / MRI
- Tissue diagnosis: ***possible***
  - EUS-FNA > ERCP
  - Reasonable to perform ERCP tissue acquisition in those needing biliary decompression

52

WHAT IS THE ROLE OF ERCP IN PANCREATIC CANCER?

- MAIN ROLE:
  - Biliary Decompression in surgically unresectable disease



53

CASE CONTINUED...

EUS reveals a 3 cm mass in the pancreas that abuts the portal vein - potentially resectable. He is referred to surgery. The patient has history of CAD. The surgeon and patient are reluctant to proceed with a Whipple operation unless a diagnosis of cancer is confirmed. How should this mass be biopsied?

(1) CT guided bx

(2) ERCP

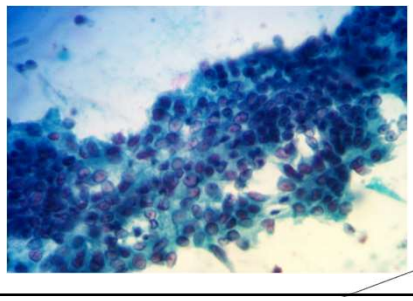
(3) EUS-FNA ←

54

EUS FNA/FNB

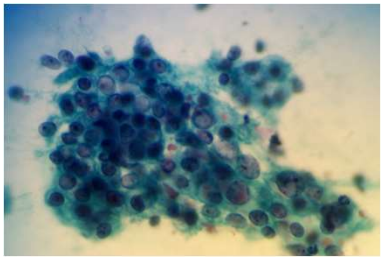
55

PATHOLOGY



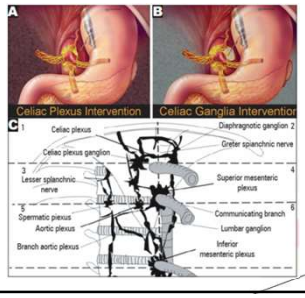
56

PATHOLOGY



57

EUS USED FOR PAIN RELIEF WITH CELIAC PLEXUS NEUROLYSIS



58

CELIAC PLEXUS NEUROLYSIS

59

SUMMARY OF TREATMENT

- Resection is the only chance for a cure, and resectable patients should undergo surgery without delay followed by adjuvant therapy
- Borderline resectable patients may benefit from neoadjuvant therapy and then surgery
- Unresectable patients may benefit from chemotherapy or chemoradiation
- Metastatic disease may benefit from chemotherapy or other palliative treatments

60


THANK YOU