

實證醫學病例討論

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clinical scenario-基本資料及主訴

- General data: 72 year-old man, underlying with diabetes mellitus, hypertension, peptic ulcer disease
- C.C : intermittent epigastragia for 4 months

Brief history

- 97/11-97/12
- He suffered from epigastragia with radiation to back, post-prandial pain. Yellowish skin and tea-color urine were also noted. Abdominal CT revealed distal CBD stone and biliary tree dilatation. PTGBD was arranged to relieve jaundice. CBD stones were extracted during ERCP and EST. Follow up fistulography showed no filling defect but CBD dilated. Then he received regular follow up at HBS-OPD.

Brief history

- 98/4-98/5
- Episodes of intermittent back pain were noted. There were no aggravating and relieving factors. He noted that his urine became tea color but no clay colored stool and also noted epigastric distention. Neither fever nor nausea/vomiting were noted.
- MRCP showed CBD wall thickening. Due to the symptoms persisted, he admitted to HBS on 98/05. ERCP showed CBD dilatation and bilateral biliary tract dilatation with sluges; cystic duct stone was suspected. Endoscopic ballon dilatation was done and due to improved symptom/signs, patient discharged.

Brief history

- 98/6-98/7
- RUQ tenderness, fever and chills were noted. The other symptom/signs included body weight loss(2~3 kgw/3 months) and DM with poor sugar control. Labs revealed obstructive jaundice.
- Pancreatic head lesion was suspected. We want to arrange a study for diagnosis.

提出background questions

Question

- How does pancreatic cancer present ?
- What is his differential diagnosis ?
- What is its diagnostic test ?

History

- **Chief Concern (CC):**
- 67-75% pain (abdominal pain, back pain, postprandial), 56-60% weight loss, anorexia, nausea, vomiting, malaise, weakness, diarrhea
- **Past Medical History (PMH):**
- 10% migratory thrombophlebitis (Trousseau's phenomenon, tissue thromboplastic factor, consider diagnosis of pancreatic carcinoma if DVT and increased PTT), new-onset diabetes or DM poor control

History

- **Social History (SH):**
- cigarette smoking
- toxic chemicals
- DDT
- **Review of Systems (ROS):**
- steatorrhea

Physical

- **General Physical:**
- with cancer in head of pancreas - 75% weight loss and obstructive jaundice, 25% back or vague abdominal pain, 20% abdominal mass, < 50% enlarged nontender gallbladder
- **Skin:**
- 65% jaundice (if head of pancreas obstructs bile duct, only 10% with body or tail cancer)
- **Abdomen:**
- palpable epigastric mass, rarely distended palpable gallbladder (Courvoisier's sign)

Differential diagnosis

- **Rule out:**
- ampullary cancer (carcinoma of ampulla of Vater, better prognosis than pancreatic cancer)
- duodenal cancer
- cholangiocarcinoma
- lymphoma
- islet cell tumor
- sarcoma
- adenoma
- sclerosing pancreatitis (also called autoimmune pancreatitis)
- mucin-hypersecreting bile duct neoplasm
- branch duct intraductal papillary-mucinous neoplasm without mural nodules

Testing to consider:

- estimates of diagnostic accuracy for pancreatic cancer
 - **ultrasound** has 70% sensitivity, 85% specificity, positive likelihood ratio 4.7, negative likelihood ratio 0.35
 - **computed tomography** has 85% sensitivity, 90% specificity, positive likelihood ratio 8.5, negative likelihood ratio 0.17
 - **angiography** has 75% sensitivity, 80% specificity, positive likelihood ratio 3.8, negative likelihood ratio 0.31
 - Reference - [BMJ 2002 Feb 23;324\(7335\):477](#)

Blood tests:

- CEA and oncofetal antigens for follow-up, 80% increased AP, increased LDH, increased SGOT, 25% increased amylase, 80% CA19-9
- **cancer antigens 19-9 and 125 may predict cancer in pancreatic mass lesions**

提出foreground questions

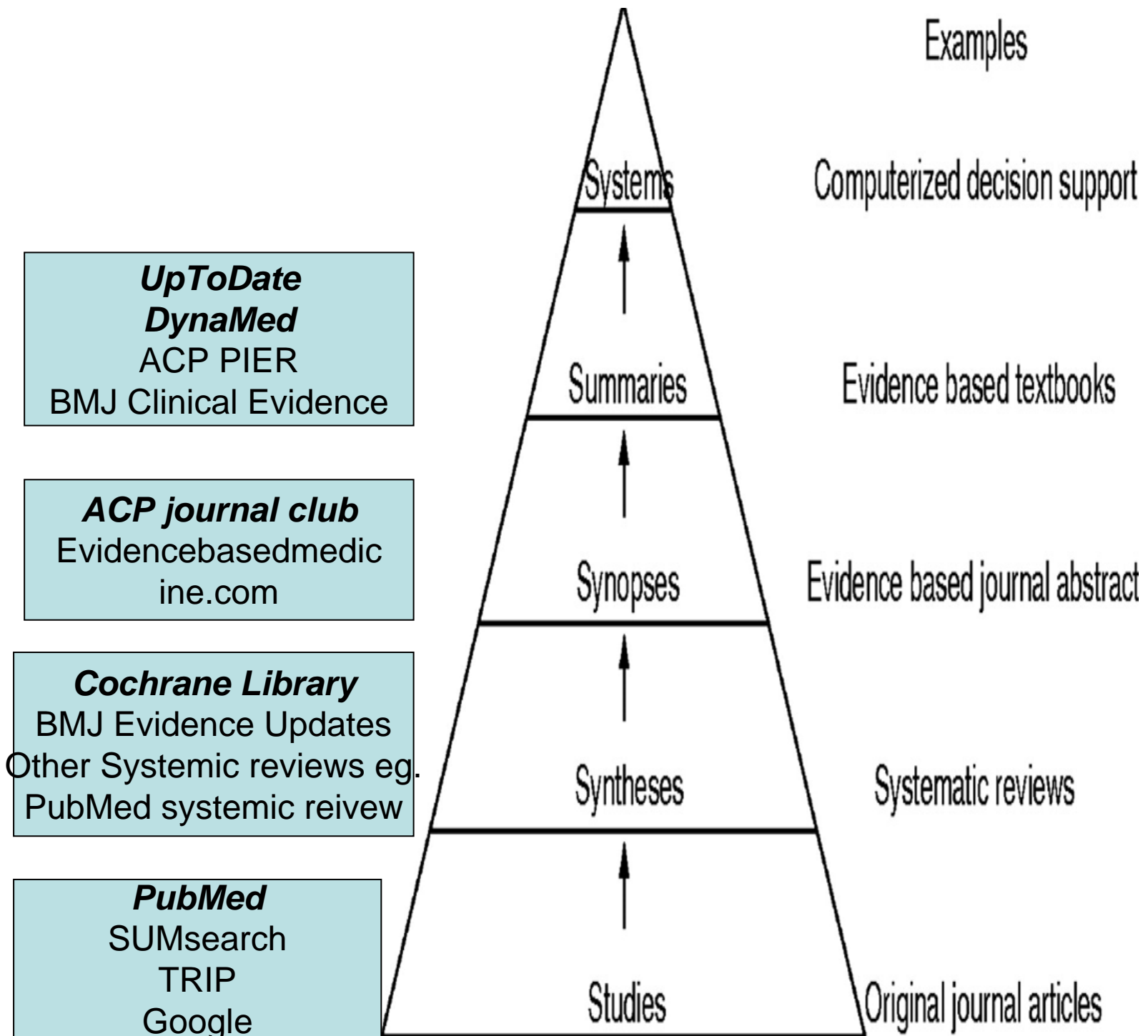
在診斷early pancreatic cancer, EUS 是否比其他
image 系統好用？

將問題寫成PICO

Patient	A patient suspect pancreatic cancer
Intervention	Endoscopic ultrasonography
Comparison	CT ; MRI/MRCP ; PET
Outcome	Sensitivities , specificities, diagnostic values

搜尋最有用的資料

先從已經過評讀的**database**開始找起
(**system,synopses,synthesis**)
最後再找尚未經過嚴格評讀的**study**



搜尋Summaries

- Up to date
- Key word : pancreatic cancer
- Topic : **Clinical manifestations, diagnosis, and surgical staging of exocrine pancreatic cancer – Image studies**

搜尋到的文章內容

- **EUS —**
- EUS is very **operator-dependent**; as a result, its value varies with locally available expertise.
- EUS appears to be most useful for diagnosis of **small tumors** (eg, **less than 2 to 3 cm in diameter**) and may also be helpful for evaluating the possibility of **nodal and major vascular involvement** except for the superior mesenteric vein and artery. **(level 2 [mid-level] evidence)**

- Diagnostic studies for pancreatic cancer

Test	Sensitivity	Specificity	Useful in staging
Ultrasound	80	90	no
Endoscopic ultrasound	90	90	yes
CT scan	90	95	yes
ERCP	90	90	no
MRCP	90	90	no
FNA	90	98	no

搜尋Summaries

- Dynamed
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- Topic : **Pancreatic carcinoma -- Testing to consider – Image studies**

搜尋到的文章內容

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搜尋到的文章內容

- **endoscopic ultrasound may be more accurate than multidetector CT for tumor detection and staging (level 2 [mid-level] evidence)**
- (Ann Intern Med 2004 Nov 16;141(10):753)
- Ann Intern Med 2005 Apr 5;142(7):590

Main results

- prospective study of 120 patients with known or suspected nonmetastatic pancreatic cancer, patients had endoscopic ultrasound then multidetector CT, patients with potentially resectable cancer on either test were considered for surgery; radiologists were not blinded to prior imaging results; 104 patients (87%) had both endoscopic ultrasound and CT, 80 patients had pancreatic cancer (27 managed without surgery, 53 had resectable tumor, 28 surgical patients had unresectable tumor);
- among 80 patients with cancer, sensitivity for pancreatic mass was 98% with endoscopic ultrasound vs. 86% with CT ($p < 0.012$);
- among 53 surgical patients, endoscopic ultrasound superior to CT for tumor staging accuracy but equivalent for nodal staging accuracy and determination of resectability

Main results

- endoscopic ultrasound had **95% sensitivity** and **53% specificity** for pancreatic cancer in series of 115 patients who had surgical biopsy of focal pancreatic lesions, 70% prevalence of pancreatic cancer and limitation of subjects to patients referred for surgery limits conclusions
- (Scand J Gastroenterol 2000;35:1221)

搜尋Synopsises , ACP Journal Club

- Key word : pancreatic cancer
- review of contrast-enhanced ultrasonographic findings in pancreatic tumors can be found in [Int J Med Sci 2008 Jul 9;5\(4\):203 full-text](#)
- Finnish Medical Society Duodecim evidence-based guideline on indications and preparation of patient for ultrasonographic examinations can be found at [National Guideline Clearinghouse 2007 Mar 19:10478](#)

搜尋Studies, Pubmed

- Key word:
- (“Pancreatic cancer”[Mesh] AND “Diagnostic image ”[Mesh]) AND “Radiographs”[Mesh]
- Limit: human ,adult ,time: since 2007

搜尋到的文章內容

- Pancreatic cancer—EUS and early diagnosis
- Lars Helmstaedter & Juergen Ferdinand Riemann
- Medical Department C, Klinikum Ludwigshafen gGmbH, Academic Hospital of the Johannes Gutenberg-University of Mainz
- Langenbecks Arch Surg (2008) 393:923–927
- 用多篇RCT所做成的綜合性分析(SR of RCTs)(Level I)

Abstract

- The highest accuracy in assessing extent of primary tumour, locoregional extension, vascular invasion, distant metastasis, tumour TNM stage and tumour resectability seems to have helical CT, whereas **EUS** has the highest accuracy in assessing **tumour size** and **lymph node involvement**.

Abstract

- several reasons for failure, and it shows a **high interobserver variety** even among experienced endosonographers. Nevertheless, EUS proved to have a **high negative predictive value**.

Table 1 Indications for EUS exam

Persistent epigastric and/or back pain

Acute onset of diabetes in the elderly

Unexplained weight loss

Acute or chronic pancreatitis

Suspect results in other imaging modalities

One of the above, especially in individuals over 45 years of age and in high-risk individuals (e.g. persons with a strong family history of pancreatic cancers, with Peutz-Jeghers syndrome (PJS) or multiple endocrine neoplasia (MEN))

Table 2 Results for accuracy of EUS in literature

	Accuracy (%)
Legmann et al. [6]	93
Akahoshi et al. [7]	94
Cannon et al. [8]	78
Ahmad et al. [9]	69
Meining et al. [10]	72
Soriano et al. [11]	63

Abstract

- Regarding **sensitivity**, determining **tumour size** and **extent**, **lymph node involvement** and **vascular infiltration**, **EUS was superior or at least equal to other imaging modalities** like computed tomography (CT) or magnetic resonance imaging (MRI) in most studies

Abstract

- If tissue diagnosis is necessary before therapy, **EUS-guided FNA** should be the method of choice.
- A EUS–FNA is highly sensitive (84%), specific (97%), accurate (84%) and has **a high positive predictive value (99%)**, but **negative predictive value is low with only 64%** → *If pancreatic cancer is suspected and if EUS–FNA is negative, cancer cannot be excluded, and operation will be the next step despite a positive or negative result in FNA.*

- Screening for pancreatic cancer and its precursor lesions in the general population is not feasible, but **high-risk subpopulations** seem to be suitable targets for screening programs
- EUS is **an essential tool** for **diagnosis** and **assessment of extension and resectability of pancreatic tumours**

Results

- The EUS- and CTbased approach found **eight patients among 78 high-risk individuals** with pancreatic neoplasms confirmed by surgery or FNA
- **No** pancreatic neoplasia among **149 control subjects**.
- For assessment of **tumour resectability**, a **combination of CT and EUS** seems to be the procedure with the highest accuracy.

搜尋到的文章內容

- A Prospective Evaluation of an Algorithm Incorporating Routine Preoperative Endoscopic Ultrasound-Guided Fine Needle Aspiration in Suspected Pancreatic Cancer
- [*J Gastrointest Surg \(2007\) 11:813–819*](#)
- Yield of Endoscopic Ultrasound–Guided Fine-Needle Aspiration Biopsy in Patients with Suspected Pancreatic Carcinoma
- [*CANCER \(CANCER CYTOPATHOLOGY\) October 25, 2003 / Volume 99 / Number 5*](#)

Table 3 Initial Cytopathology and Final Diagnosis of Solid Pancreatic Mass Lesions

EUS-FNA Cytology	Final Diagnosis			
	Benign	Malignant	Indeterminate/ Unknown	Total
Benign	91	17	3	111
Atypical	8	15	1	24
Suspicious	1	22	2	25
Malignant	2	379	0	381
Failed/inadequate	1	4	1	6
Total	103	437	7	547

Results

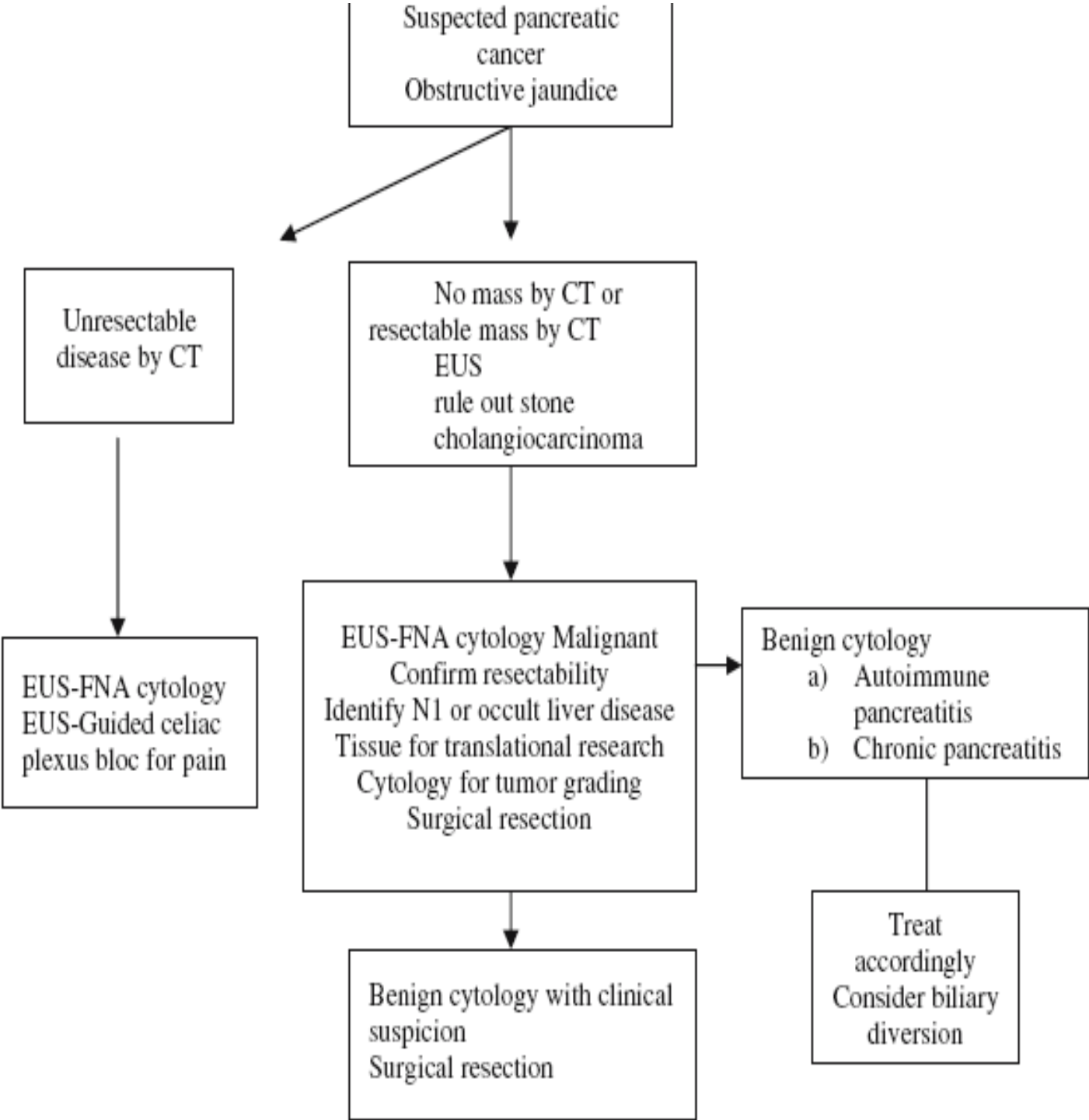
- Of 547 patients enrolled (median age 64 years, 60% male), 49% presented with obstructive jaundice.
- The operating characteristics of EUS-FNA of solid pancreatic masses were: sensitivity 95% (95% CI: 93.2–95.4), specificity 92% (95% CI: 86.6–95.7), positive predictive value 98% (95% CI: 97–99), negative predictive value 80% (95% CI: 74.9–82.7).
- The overall accuracy of EUS-FNA was 94.1% (95%CI: 92.0–94). Of the 414 true positive patients by EUS-FNA, 138 (33%) were explored.

Results

- Of patients deemed operable by combined imaging, 42% had surgical resection. **Eighty-two percent of true positive** patients were ultimately found inoperable and received **palliative therapy or chemotherapy**.
- Of the **94** patients with **true negative** cytology based on extended follow-up, **only 7 (7%) underwent surgical resection**. Of those with **false negative** diagnoses (**n=24**), 5 patients underwent exploration/resection based on detection of mass lesions by EUS. The remaining patients had unresectable disease.
- Mild self-limiting pancreatitis occurred in (0.91%).

- EUS-FNAB is a safe and highly accurate method for tissue diagnosis of patients with solid pancreatic lesions. Patients with suspicious and atypical EUS-FNAB aspirates deserve further clinical evaluation.

for EUS-FNA based approach
in patients with suspected pan-
creatic cancer.




Appraisal (嚴格評讀)

對找到的文章
進行critical appraisal

證據等級(針對PubMed這篇)

Level	與[治療/預防/病因/危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見



將文獻寫成PICO

Patient	A patient with obstructive jaundice suspect pancreatic cancer
Intervention	Endoscopic ultrasonography with FNA
Comparison	no
Outcome	Sensitivities , specificities, diagnostic values

• **Critical Appraisal of Diagnostic Accuracy Study**

• “診斷工具”的評析

- • Are the results of the study valid (效度如何) ?
Narrow confidence interval
- – Was the diagnostic test evaluated in a representative spectrum of patients (是否經過具有代表性的病人群測試過) ? Yes
- – Was the reference standard ascertained regardless of the index test result (標準診斷工具做確診時不知道指標診斷工具的結果) ? no
- – Was there an independent, blind comparison between the index test and an appropriate gold standard of diagnosis (標準診斷工具與指標診斷工具是在獨立且雙盲的情況下進行比較) ? no
- Are test characteristics presented (呈現指標診斷工具的特性) ? Yes
- Can we apply to our patient (可以應用到我的病人嗎) ?
Yes

- sensitivity 95% (95% CI: 93.2–95.4), specificity 92% (95% CI: 86.6–95.7), positive predictive value 98% (95% CI: 97–99), negative predictive value 80% (95% CI: 74.9–82.7).

- LR +

$$\text{Sensitivity} / 1 - \text{specificity} = 95 / 1 - 92 = 11.875$$

- Pre-test odds = prevalence / (1 - prevalence)

$$0.8 / 0.2 = 4$$

- Post-test odds = pre-test odds X likelihood ratio

$$- 4 \times 11.875 = 47.5$$

Summary

- EUS-FNA is benefit for this patient, and we arrange EUS-FNA for him.
- But results of EUS-FNA showed negative.
- We arrange operation(Whipple operation) for him and final diagnosis showed pancreatic ductal adenocarcinoma.

Thank you for attention!