

# Résumés des communications libres / Abstracts of free communications

## Predictive factors of malignancy of mediastinal lymph nodes (LN) in a consecutive series of patients referred to a tertiary center for EUS FNA

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### AIM

To assess the predictive factors of malignancy of mediastinal LN in a consecutive series of patients referred for EUS FNA in a tertiary care centre.

between benign and malignant LN were compared with Student's *t* test and Chi-square test respectively. Received operating curves (ROC) were made for each set of criteria and for LN size to assess their capability to predict metastatic LN.

### STUDY POPULATION AND METHODS

Data from all consecutive patients referred from January 2001 to May 2004 for diagnosis or staging of the mediastinum in whom EUS FNA was performed, were collected. Computed variables were the following: age, gender, presence of malignancy and LN characteristics such as location, size (long and short axis), echogenicity (hypoechoic vs non-hypoechoic), shape (round vs non-round) and borders (sharp vs non-sharp).

EUS was performed under conscious sedation with a radial echoendoscope (Olympus GF UM20 and GF UM160) to assess LN features. A linear echoendoscope (Olympus GF UC30P) and a 22-gauge needle (Wilson Cook Medical, Inc.) were then used in order to perform EUS FNA of the evaluated LN. Cytology obtained from EUS FNA was used as gold standard. LN with an uncertain diagnosis or those from which a diagnostic sample could not be obtained had been excluded for the analysis. Variables concerning LN were grouped in different sets of criteria: 1) classic criteria (ClCr): short axis 1 cm or larger, round shape, homogeneous hypoechoic pattern, sharp and distinct borders; 2) ClCr + presence of malignancy; 3) ClCr + lung cancer; 4) ClCr + presence of malignancy + location in regions 5 and/or 7; 5) ClCr + lung cancer + location in regions 5 and/or 7; 6) short axis > 1 + presence of malignancy; 7) short axis > 1 + lung cancer; 8) short axis > 1 + presence of malignancy + location in regions 5 and/or 7; 9) short axis > 1 + lung cancer + location in regions 5 and/or 7. Size (short and long axis) and shape, echographic patterns and borders

### RESULTS

112 LN were evaluated in 73 patients (68 M/5F), with a mean age of  $63 \pm 9$ . Fifty nine patients (81 %) were evaluated for staging of a known malignancy (lung cancer  $n = 50$ , esophageal cancer  $n = 6$  other neoplasms  $n = 3$ ), and the remaining 14 (19 %) for diagnostic purposes. Thirty nine LN were excluded for inconclusive cytologic diagnosis. Of the analysed 73 LN, 47 (64 %) were benign and the remaining 26 (36 %) malignant by means of cytology obtained by EUS FNA. Location of the LN was as follows: station 7,  $n = 28$  (38 %); station 8,  $n = 17$  (23 %); station 5,  $n = 16$  (22 %); and others,  $n = 12$  (17 %).

Long and short axis of the LN and hypoechoic pattern were the only variables significantly different between benign and malignant LN ( $1.1 \pm 0.6$  vs  $2.7 \pm 1.7$  and  $0.7 \pm 0.4$  vs  $1.7 \pm 1$ , respectively,  $p = 0.001$ ). ROC showed an area under the curve (AUC) of 0.71 for the ClCr and  $< 0.8$  for all sets of other criteria but one (short axis of the LN > 1 + malignancy: AUC = 0.86). However, size of the LN as assessed by the short axis as a quantitative variable showed the best AUC (= 0.91; 95 % CI 0.85, 0.98).

### CONCLUSIONS

Short axis of the LN is the best predictor of malignancy in mediastinal LN. As a set of criteria, short axis of LN > 1 cm + the presence of a malignancy is a better predictor of metastatic LN than the classic EUS criteria.

# Endoscopic ultrasonography (EUS) vs magnetic resonance cholangiopancreatography (MRCP) in the diagnosis of pancreatobiliary disturbances with and without dilated biliary tract : definitive results of a prospective, blinded and comparative study

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## AIMS

To prospectively and blindly compare the performance characteristics of EUS and MRCP : 1) in the etiologic diagnosis of the dilated biliary tract and 2) in the diagnosis of choledocolithiasis in patients with non-dilated biliary tract.

## STUDY DESIGN AND METHODS

From March 2001 to June 2004, patients meeting one of the following inclusion criteria were prospectively enrolled : 1) Unexplained common bile duct dilation in transabdominal ultrasound (US) (Group I; n = 74) and 2) High suspicion of choledocolithiasis (fever, abdominal pain and hepatic tests impairment or acute pancreatitis of probable biliary origin) with a non-dilated biliary tract on US (Group II; n = 79). Patients with personal history of claustrophobia or gastroenteroanastomosis and peace-maker carriers were excluded. Radial EUS (Olympus GF UM20 and GF UM160) and MRCP with SSFSE technique were performed within a 24-hour period. The sequence of the two techniques was randomly assigned and the operators were blinded with respect to the results of the other procedure. Gold standard was endoscopic retrograde cholangiopancreatography (ERCP) (n = 89), surgery with intraoperative cholangiography when needed (n = 24) or clinical follow-up (n = 35).

## RESULTS

153 patients (67 men, 86 women) with a mean age of  $68 \pm 15$  were included. Mean time between EUS/MRCP and ERCP or surgery was  $11 \pm 13$  and

$30 \pm 31$  days respectively. Mean follow-up in patients in whom this was considered as gold standard was  $5.8 \pm 3.9$  months. Two patients in Group I and four in Group II were considered lost before a definitive diagnosis (death for other reasons n = 3, lost of follow-up n = 3). EUS could not be performed in 6 patients for severe medical problems after inclusion (n = 4), non-reported history of surgery (n = 1) or stenosis of the digestive tract (n = 1), whereas MRCP could not be completed in 7 patients for unexpected claustrophobia. Therefore, a total of 65 and 69 patients were evaluated in Groups I and II respectively for the analysis. Final diagnosis was choledocolithiasis (Group I/II : n = 36/30), cholelithiasis without choledocolithiasis (Group I/II : n = 8/38), pancreatic cancer (Group I/II : n = 18/3), cancer of the biliary tract (Group I/II : n = 5/3), chronic pancreatitis (Group I/II : n = 2/0) and others (Group I/II : n = 1/1). Performance characteristics of EUS and MRCP in the two study groups are showed in the following table :

	Group I					Group II				
	Se	Sp	PPV	NPV	Acc*	Se	Sp	PPV	NPV	Acc
EUS	100 %	71 %	97 %	100 %	97 %	91 %	78 %	78 %	91 %	84 %
MRCP	88 %	71 %	96 %	42 %	86 %	87 %	92 %	90 %	89 %	90 %

\* Mc Nemar's test :  $p < 0.05$

## CONCLUSIONS

EUS and MRCP are good techniques for the diagnosis of pancreatobiliary disturbances in patients with and without biliary tract dilation. EUS is more accurate than MRCP for the etiologic diagnosis in patients with dilation of the biliary tract.

# **Etude prospective sur l'exactitude d'une analyse cytologique immédiate par l'échoendoscopiste, de ponctions à l'aiguille fine (PAF)**

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## *INTRODUCTION*

Le rendement de la PAF est accru par la présence du cytopathologiste en salle. Ceci est toutefois impossible dans de nombreux centres où l'échoendoscopiste est alors confronté à 2 choix : augmenter le nombre de passages en majorant les complications ou limiter son nombre au prix de faux négatifs.

## *BUT*

A partir d'une étude prospective monocentrique, évaluer l'efficacité de l'échoendoscopiste à déterminer la cellularité d'échantillons immédiatement après la ponction de masses solides ainsi que son impact sur la procédure finale.

## *PATIENTS ET MÉTHODES*

Cent patients consécutifs ont été inclus avec indication de PAF pour masse solide pancréatique, masse médiastinale ou ganglion. Un minimum de 2 passages par cible était fait sauf en cas de problème technique. Une lame par passage, celle jugée la moins cellulaire par l'opérateur était immédiatement colorée au bleu de toluidine. La lame était évaluée macroscopiquement puis au microscope pour évaluer la cellularité (O/N). Immédiatement après le passage, l'opérateur devait préciser si le prélèvement aurait été jugé suffisamment adéquat pour cesser la ponction dans un contexte non expérimental. En cas d'absence de cellularité après les 2 passages, d'autres passages étaient permis ( $\leq 5$ ) jusqu'à l'obtention de cellularité ou la survenue d'un problème technique. Des cytoblocs étaient faits avec le reste du matériel chaque fois que possible. Tous les prélèvements étaient ensuite évalués dans un autre centre par le cytopathologiste. Les

résultats des opérateurs et du cytopathologiste étaient ensuite comparés quant à l'appréciation de la cellularité. Le diagnostic final des masses médiastinales et pancréatiques a été confirmé par chirurgie ou lors du suivi. Il n'a pas été précisé pour les ganglions en raison du manque de spécimens chirurgicaux.

## *RÉSULTATS*

Entre 10/2003 et 06/2004, chez 100 patients (60 hommes, âge moyen 65,3 ans) inclus, 112 cibles (diamètre moyen 27 mm (6-60)) ont été ponctionnées (73 pancréas, 34 ganglions, 5 masses médiastinales). 220 passages ont été faits pour un total de 597 lames et 147 cytoblocs. L'évaluation de la cellularité par l'opérateur avant et après coloration était de 70 % et 80 %. Ceci était corrélé dans 80 % des cas avec la cellularité estimée par le cytopathologiste. En cas d'erreur, on notait une difficulté de jugement des échoendoscopistes dans 65 % des cas. L'exactitude finale des ponctions pour masses malignes du pancréas et du médiastin était de 86 %. Dans un contexte non expérimental, un seul passage aurait été effectué chez 42 patients. Dans ce groupe, l'exactitude du premier passage était de 86 % et l'exactitude finale était de 89 %.

## *CONCLUSION*

L'évaluation de la cellularité des lames par les échoendoscopistes a une bonne concordance avec l'analyse du cytopathologiste. Lorsque la cellularité est jugée satisfaisante au premier passage, des passages additionnels ne sont probablement pas nécessaires.

## What is the right timing of EUS examination for assessing response to neoadjuvant therapy ?

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*The assessment of response to neoadjuvant chemoradiotherapy (NCRT) is a very important issue for multimodal treatment of esophageal carcinoma. EUS has been proposed as a reliable tool in evaluating such a response, by measuring the maximal cross sectional area (MCA) of the tumor, before and after neoadjuvant therapy. It has been reported that a positive pathologic response can be predicted when a reduction greater than 50 % of MCA is recognized by EUS. However this method is not immune to criticisms; one concerns the lack of a definite timing of EUS after NCRT. It has been only claimed that an interval of at least 4 weeks after the end of neoadjuvant therapy is advisable, in order to minimize chemoradiation induced reaction.*

*The aim of this study was to establish whether four weeks are the right interval of time to perform EUS after the NCRT. For this purpose fifteen consecutive patients with esophageal cancer, candidates to multimodal therapy because of a locally advanced disease, according to pre-treatment EUS staging, were submitted to two successive EUS examinations after NCRT. The first was scheduled for the 3<sup>rd</sup> week, the second for*

*the 6<sup>th</sup> week after the end of neoadjuvant therapy. EUS after 3 weeks showed a reduction of MCA greater than 50 % (EUS positive response) in 12 pts and a lesser than 50 % reduction (EUS negative response) in 3 pts. None of the patients had EUS response changed at the second examination after NCRT. Apart from a single patient who showed an additional 20 % reduction, compared with initial EUS, no substantial modifications of MCA occurred in the other patients. Only slight variations, indeed, were found in terms of a decreasing in tumor size, from 0.5 to 8 % (11 pts), or in terms of an increasing, from 1 to 4 % (3 pts).*

*It is debatable whether such variations are only due to limitations of measurement method or can be related to NCRT effects (residual cytoreductive action or further regression of reactive phenomena). Considering that most of the reduction of tumor size has been already achieved after 3 weeks, it is possible to conclude that 4 weeks are really the right timing of EUS after NCRT. Probably it would not matter if one or two more weeks were waited, but it is better to utilize this time for performing subsequent therapy (palliative chemoradiation or surgery).*

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## Immunocytochemistry as an ancillary technique in evaluation of EUS-guided fine needle aspiration biopsy : our experience

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*EUS-guided fine needle aspiration biopsies (EUS-FNAB) has significantly increased the diagnostic capability of EUS. A retrospective analysis of experience with FNA sampling and cytopathological diagnosis in our Institute is reported.*

**METHODS :** *One hundred and ten patients from January 2001 to October 2004 underwent EUS-FNA. Presenting symptoms included the following : pain, weight loss, altered bowel habits, nausea/vomiting, palpable mass. Some patients had a previous diagnosis of cancer (colon, kidney).*

*EUS-FNAB procedures were carried out using a 22-gauge needle. An experienced cytopathologist was present during FNA in all cases, making an extemporaneous evaluation of the adequacy of the sample.*

*Our casuistic is mostly constituted from EUS-FNAB of pancreatic masses (64 cases), gastric lesions (19 cases), intraabdominal, retroperitoneal, mediastinic nodes (the remaining).*

*Execution of simultaneous double sampling (pancreatic or gastric masses plus adenopathy) was also possible in some cases for preoperative evaluation of metastatic diffusion.*

*Immunocytochemistry on cell block material was performed in order to : clarify the diagnosis when the morphology alone was not sufficient ; demonstrate the neuroendocrine (NE) differentiation ; evaluate the proliferation index ; study immunophenotype and monoclonality in cases of lymphomas ; influence decisions regarding therapeutic strategies (somatostatin receptors in NE tumours, CD117 in GIST). Suspected lymphoproliferative lesions were analyzed by flow cytometry and/or molecular biology methods to detect clonal expansion of B or T-cell origin.*

**RESULTS :** *A final cytological diagnosis by EUS-FNAB was performed in 90/110 patients, while in 20/110 cases the material was not sufficient.*

*Immunohistochemistry with different panels of antibodies was performed in 25/90 cases.*

*The positive diagnoses included three Neuroendocrine pancreatic lesions, seven gastric stromal fusocellular neoplasms (GIST), four lymphomas, three lymph nodal metastases.*

*In some of the twenty one pancreatic adenocarcinomas, Chromogranin A detection was performed to exclude a NE component.*

## CONCLUSIONS

*The EUS-FNA FNAB procedure is a useful tool for diagnosing intraabdominal masses. Immunohistochemical staining performed on cell block material can improve the diagnostic accuracy and give therapeutic suggestions.*

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# **L'échoendoscopie (EE) est-elle suffisante pour éliminer les tumeurs kystiques du pancréas à potentiel malin ? Suivi de 163 patients asymptomatiques**

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## INTRODUCTION

Si la chirurgie reste le traitement de référence des tumeurs kystiques à potentiel malin (TKM), une surveillance peut être proposée pour les tumeurs kystiques à potentiel bénin (TKB) comme les cystadénomes séreux (CS) ou les kystes congénitaux (CC). Cependant, le diagnostic de TKB reste difficile à affirmer. En 1991, nous avons défini les critères en EE permettant de conclure à une TKB. Nous présentons maintenant la plus grande série de surveillance de patients sélectionnés selon ces critères afin de confirmer leur efficacité pour le diagnostic des TKB.

aiguë ou chronique étaient exclus. Il s'agissait de 121 femmes et 42 hommes d'âge moyen 65 ans (14-84). L'EE concluait à 101 CS, 43 CC et 19 kystes multiples. La taille moyenne des kystes était de 21 mm ; ils étaient de siège corporéo-caudal pour 48 patients. Un suivi clinique et radiologique était recommandé aux patients et à leur médecin. Les patients ou les médecins traitant ont été recontactés tous les 3 ans afin de collecter les informations sur l'existence de symptômes, la réalisation d'une chirurgie pancréatique et sur l'évolution des kystes aux examens morphologiques. La dernière évaluation a été faite de février à avril 2004.

## PATIENTS ET MÉTHODES

De juin 1992 à novembre 1996, 163 patients consécutifs, asymptomatiques et suspects de TKB à l'EE ont été inclus. Les patients présentant des signes de pancréatite chronique ou une histoire de pancréatite

## RÉSULTATS

8 patients furent opérés d'emblée à la demande de leur médecin : la TKB était confirmée pour tous (7CS, 1CC) ; 11 patients (7 %) étaient perdus de vue en 2004 ; 144 ont finalement été suivis. 34 sont

décédés pendant le suivi dont un seulement d'une tumeur neuroendocrine caudale alors que la TKB était céphalique. 4 patients devenus symptomatiques ont été opérés avec confirmation du diagnostic initial (3CS, 1CC) ; 106 patients restaient asymptomatiques avec un suivi clinique moyen de 9 ans. Un suivi radiologique a été réalisé chez 98 patients, comportant 421 explorations (248 échographies, 52 TDM, 113 EE, et 12 ponctions). Des signes morphologiques en faveur d'une TKM sont apparus chez 10 patients (8 EE, 2 TDM). 8 furent opérés avec 6 diagnostic de TKM (3 cystadénomes mucineux et 3 TIPMP) et 2 de TKB (1CS, 1CC) ; 2 patients sont suivis. L'évolution de la taille des lésions n'était pas un critère suffisant pour suivre les patients car la stabilité, l'augmenta-

tion ou la diminution était observée aussi bien dans les TKM que dans les TKB.

### CONCLUSION

Dans cette étude de suivi les critères écho endoscopiques ont été efficaces pour le diagnostic de TKB avec l'absence de dégénérescence apparue avec un suivi moyen de 9 ans. 5 % des patients étaient cependant finalement porteurs de tumeurs à potentiel malin. Un suivi reste donc nécessaire, idéalement par EE. Le suivi de la taille est insuffisant. L'intérêt d'une ponction du kyste avec cytologie et dosage des marqueurs tumoraux reste à prouver dans cette population.

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## Utility of power Doppler endoscopic ultrasound for the differential diagnosis between pancreatic cancer and pseudotumoral chronic pancreatitis

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*Endoscopic ultrasound (EUS) coupled with fine needle aspiration biopsy (EUS-FNA) are very useful for the detection of pancreatic tumors, for the differential diagnosis between benign and malignant tumors, as well as for staging and resectability. However, the accuracy of EUS and EUS-FNA for the differential diagnosis of pancreatic masses are variable in the literature being as low as 75 % in some studies.*

*Our study included 42 consecutive patients with a clinical suspicion of pancreatic tumor masses (27 men and 15 women), examined by EUS, between January 2002 and August 2004. EUS procedures included color and power Doppler, as well as EUS-FNA in all patients. Final diagnosis of pancreatic cancer was confirmed in 29 patients based on a combination of information provided by imaging tests, clinical follow-up of 6 months, as well as laparotomy in 18 patients for diagnostic or palliative reasons.*

*Sensitivity and specificity of the absence of power Doppler signals inside the suspicious pancreatic mass were 93 % and 77 %, with an accuracy of 88 %. Moreover, the addition of the information provided by the presence of peripancreatic or periduodenal collaterals improved the sensitivity and specificity to 97 % and 92 %, with an accuracy of 95 %.*

*In conclusion, power Doppler EUS provides useful information for the differential diagnosis of pancreatic masses. The results of our study are in concordance with previous studies that demonstrated a hypovascular pattern of pancreatic carcinoma, as well as the formation of collaterals in advanced cases due to the invasion of the splenic or portal veins. Further studies of dynamic EUS with contrast agents are necessary to better characterize pancreatic masses.*