

EFFECTIVENESS OF THE ECHOENDOSCOPIC PUNCTURE IN THE DIAGNOSIS OF SOLID PANCREATIC MASS

Efetividade da punção ecoendoscópica no diagnóstico de massa pancreática sólida

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ABSTRACT – Background – Echoendoscopy is a mixed technique which adds the advantages of endoscopy to those of transabdominal ultrasonography through an endoscope with transducer in its distal extremity, allowing for the evaluation of the abdominal organs reached by the endoscope and in contact with the intestinal wall. **Aim** - To verify the positivity rate of the echoendoscopy with puncture with thin needle (EPTN) or (EE-PAF) in solid pancreatic mass based on the technique used in the Gastrointestinal Endoscopy Unit of Hospital das Clínicas, University of São Paulo. **Methods** - Retrospective evaluation - cohort study - of 138 patients who were submitted to echoendoscopy through aspiration puncture between May 2004 and June 2007. The data were collected through the medical charts present in the medical files of Hospital das Clínicas (Clinical Hospital) of the University of São Paulo, having as inclusion criterion the presence of solid pancreatic mass in computerized tomography and as exclusion criterion the presence of non solid pancreatic tumor. The routine technique was the one used in the Gastrointestinal Endoscopy Unit focusing the following variables: mass characteristics (size, location, presence of peripancreatic lymph node, presence of lymph node in celiac trunk); number of punctures to obtain microfragment for cytology, and experience of the professional in charge. The equipment used was an echoendoscopy device model Olympus EUS (EYES) Exera EU – C60, with electronic sectorial transducer and 22 gauges Wilson-Cook needles. **Results** – Seventy six (55,4 %) male patients and 61 (44,5 %) female were enrolled. Age ranged from 16 to 87 years and means 59,9 years. The lesions were cephalic in 94 (68,1 %). Mass larger than 4 cm had a higher percentage of positivity reaching 40%, but lesions smaller than 2 cm had a percentage of 43% of inconclusive. Microfragments were obtained in 100% of the positive cases and only 73,1 % when negative (P=0,004). There was no statistic difference regarding the experience of the endoscopy professional. Only 80 patients had the number of punctures written down and it was noticed that there is better performance as the number of punctures was increased. The definitive histopathological diagnosis of pancreatic neoplasia occurred in only 41(29,7 %) patients. **Conclusions** - Regarding mass characteristics, when larger is the mass, larger is the positivity of the method; the location didn't correlate with higher positivity; when the lymph nodes were present, there was a tendency to positivity; concerning the number of punctures, the higher number, higher positivity; in relationship to the professional experience in endoscopy, there was no difference in the rate of positivity of the puncture of the solid pancreatic mass.

HEADINGS - Solid pancreatic mass. Echoendoscopy. Puncture.

INTRODUCTION

Adenocarcinoma represents 90 % of the pancreatic neoplasias. In Brazil it corresponds to 2 % of all kinds of cancers and is responsible for 4 % of the total of cancer deaths¹⁸. The frequency of this neoplasia varies according to the age, being 10 cases/100,000 in the fourth decade and 116 cases/100,000 between 80 and 85 years old. In the USA approximately 37,000 new cases are diagnosed each year, which represents the fifth death cause from neoplasia in the male population¹⁹. The world incidence is estimated in 200,000 new cases per year.

The patients habitually present obstructive jaundice, weight loss, abdominal discomfort or pain at the moment of the diagnosis, which represent most of the time an ad-

vanced stage of the disease and reserved prognosis. It is estimated that only 3.5 % of them will survive five years after the diagnosis¹⁸ and this is due to the fast evaluation of the disease involving adjacent organs and early onset of metastasis which impede the surgical resection, the only real chance of cure. This condition justifies the search for complementary diagnostic methods such as echoendoscopy, which may diagnose this illness at an early stage.

Echoendoscopy, which started with DiMagno et al.¹⁰ in the USA, Hisnaga et al.¹⁵ in Japan and Strohm et al.²⁸ in Germany, is a mixed technique which adds the advantages of endoscopy to those of transabdominal ultrasonography through an endoscope with transducer in its distal extremity, allowing for the evaluation of the abdominal organs reached by the endoscope and in contact with the intestinal wall. As of the 1990s, with Vilmann et al.²⁹ there was a development of capacity of the endoscopy to perform biopsies through punctures, even in very small lesions diagnosed by tomography or magnetic resonance, even making it possible to stage these lesions locally.

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The indication of echoendoscopy through fine needle aspiration includes biopsies of lesions, mucosa and submucosa whose conventional endoscopy couldn't produce a diagnosis. This procedure is more commonly used in periintestinal structures such as lymph nodes and pancreatic masses, hepatic, adrenal gland and biliary duct. Therefore, it is an efficient method to evaluate solid masses in the pancreatic parenchyma, since it does not present gas or abdominal fat interposition. Many authors, including Gress et al.¹⁴, Eloubeidi et al.¹¹ and Maluf F.²⁴ report that endoscopy shows sensitivity between 80 and 90% and specificity near 100% when detecting pancreatic solid lesions. Agarwal et al.¹ claim that the absence of focal pancreatic value means absence of pancreatic lesion to echoendoscopy.

Some complication may occur and the most frequent are pancreatitis and bleeding, although with incidence between 1 and 4 % and contamination of the trajectory area of neoplasia puncture, which had its first case described by Paquin et al.²⁶.

There are several studies comparing the pancreatic mass diagnostic method. Wiersema³⁰ compared echoendoscopy with computerized tomography and observed higher sensitivity and specificity in the first one. DeWitt et al.⁹ evaluated with higher sensitivity and specificity the presence of regional lymph nodes. Soriano et al.²⁷, in their turn, presented advantage of tomography as it diagnoses metastasis from a distance. However, it would be better to evaluate them with complementary exams to stage pancreatic cancer.

The retrograde endoscopic colangiopancreatography (RECP) is also used as a method to diagnose these biliary pancreatic lesions, making it possible to obtain cytological brush to anatomic pathologic analysis. However, it presents an incidence of complication which can not be disregarded as well as low sensitivity and accuracy (33.3 % and 46.7 % respectively).

On comparing echoendoscopy with magnetic resonance, Muller et al.²⁵ presented sensitivity of 94 % to echoendoscopy versus 84% on it in lesions smaller than 3 cm and specificity near 100 % to both methods. Echoendoscopy presents an advantage as it allows diagnostic puncture.

Levy^{21,22}, as well as Wiersema³⁰ highlight the fact that echoendoscopy is a method with high sensitivity and specificity to identify pancreatic mass and it presents higher cost-benefit ratio if compared to the methods described above.

This study was proposed in order to evaluate the impact of this methodology in the diagnosis of solid pancreatic mass and the evaluation of the results in this institution.

METHODS

This study involves the retrospective cohort evaluation of 138 patients who underwent echoendoscopy through fine needle aspiration puncture (EE – FNAP), having as inclusion criterion the presence of solid pancreatic mass in computerized tomography.

The interest variables of this research were: characteristics of mass (size, location, presence of peripancreatic

lymph nodes, presence of lymph nodes in celiac trunk); number of punctures to obtain microfragment and cytological material and experience of the professional who executed the procedures.

The exclusion criterion was the presence of non solid pancreatic tumor.

The research data were collected through the patient's records existing in the medical files of the Hospital das Clínicas of the University of São Paulo in the period between May 2004 and June 2007.

In the EE – FNAP procedure an Olympus echoendoscope, model Olympus EUS (EYS) Exera EU-60 with electronic sectorial transducer was used. This appliance is connected to an Olympus Exera CLV-160 processor. The needles used in the punctures were Wilson – Cook 22 gauges.

The work with the blades used the coloring technique known as Papanicolau and the fragments were set in blocks using the technique known as Cell-block. The pathologic exam followed the usual routine of the Pathology Service of the Pathologic Anatomy Department of the University. Five results were standardized in the Service: 1 – positive, included all forms of solid neoplasias; 2 – suspected, presence of cellular or architectural pattern suggesting neoplasia; 3 – undetermined, presence of representative material but which did not fit any classification of neoplasia; 4 – negative, enough material and without signs of malignancy in the sample; 5 – inconclusive, little representative material or not enough material for any diagnostic analysis.

RESULTS

Setenty six (55.47 %) were males and 61 (44.53 %) females. Their age ranged between 16 and 87 years old, with average of 59.9 and median 51.5 years.

It can be observed on Table 1 that the percentage of inconclusive diagnosis (43.2 %) tends to be higher for tumors with smaller solid pancreatic mass (up to 2 cm). This same tendency is noticed in negative results (32.4 %). On the other hand, there is a tendency to increase the positivity percentage as the pancreatic mass increases. For masses between 4 cm and 6 cm the positivity percentage reached 40.0 % (Figure1).

The qui-square test which was employed with value 0.118, did not detect association between the variables

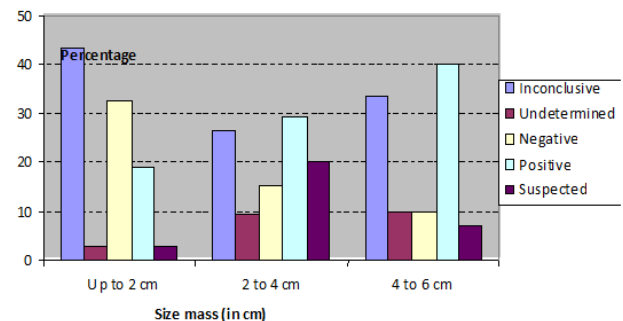


FIGURE 1 – Diagnosis percentage and mass size

TABLE 1 – Diagnosis percentage (%) and mass size*

Diagnosis	S: Mass size (cm)*			Total
	S ≤ 2	2 < S ≤ 4	4 < S ≤ 6	
Inconclusive	16 (43,2)	17 (26,2)	10 (33,3)	43 (32,6)
Undetermined	1 (2,7)	6 (9,2)	3 (10,0)	10 (7,6)
Negative	12 (32,4)	10 (15,4)	3 (10,0)	25 (18,9)
Positive	7 (18,9)	19 (29,2)	12 (40,0)	38 (28,8)
Suspected	1 (2,7)	13 (20,0)	2 (6,7)	16 (12,1)
Total	37 (100,0)	65 (100,0)	30 (100,0)	132 (100,0)

Value P=0,012 * The size of six tumors was not measured.

peripancreatic lymph nodes and diagnosis. The qui-square test with value 0.394 detected association between lymph nodes in the celiac trunk and diagnosis.

The definite neoplasia pathologic diagnosis for pancreatic neoplasia occurred only in 42 patients (29.71 % - Figure 2), being the adenocarcinoma responsible for 86.37 %, followed by the endocrine tumor (13.57 %).

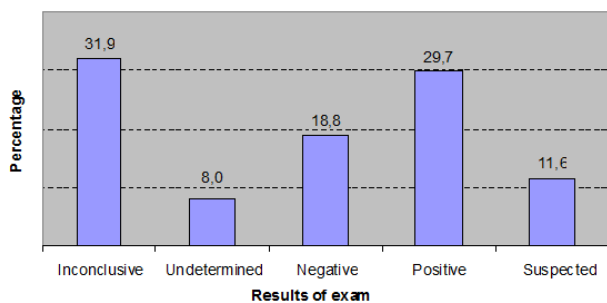


FIGURE 2 – Pathologic aspects for malignancy

The size of the sample was not sufficient to verify the existence of association between the number of punctures and the diagnosis. However, there is a tendency of higher detection of positive diagnosis as the number of punctures increases (Table 2 and Figure 3).

TABLE 2 – Frequency and percentage distribution of diagnosis and the number of punctures

Diagnosis	Number of punctures				Total
	1	2	3	4	
Inconclusive	2 (25,0)	10 (29,4)	7 (31,8)	2 (12,5)	21 (26,3)
Undetermined	1 (12,5)	3 (8,8)	0 (0,0)	3 (18,8)	7 (8,8)
Negative	3 (37,5)	7 (20,6)	5 (22,7)	2 (12,5)	17 (21,3)
Positive	2 (25,0)	8 (23,5)	8 (36,4)	6 (37,5)	24 (30,0)
Suspected	0 (0,0)	6 (17,7)	2 (9,1)	3 (18,8)	11 (13,8)
Total	8 (100,0)	34 (100,0)	22 (100,0)	16 (100,0)	80 (100,0)

Value P: insufficient sample size
Note: 58 puncture numbers were not possible to be reached

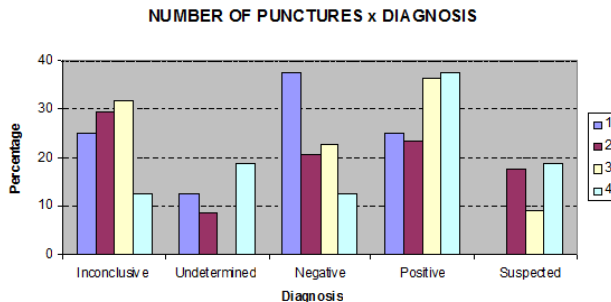
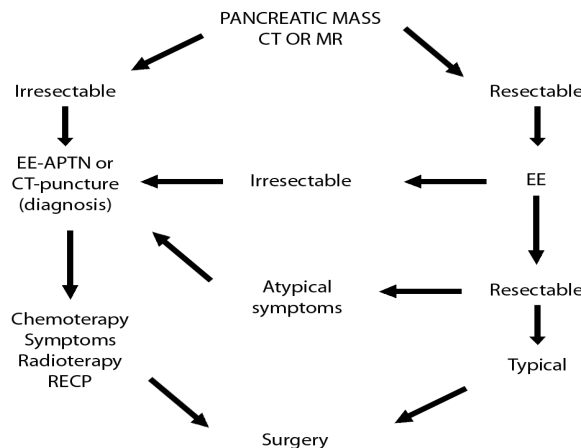


FIGURE 3 - Frequency and percentage distribution of diagnosis and the number of punctures

DISCUSSION

In this institution either the helical tomography or magnetic resonance is determined as a first exam used in the investigation of solid pancreatic mass, such as the algorithm proposed by Chaya⁸, followed by the of echoendoscopy to evaluate the resectability of the lesion (Figure 4).



Source: Chaya C, Nealon WH, Bhutani MS. EUS or percutaneous CT/US-guided FNA for suspected pancreatic cancer: when tissue is the issue. *Gastrointest Endosc.* 2006 Jun;63(7):976-8
CT = computerized tomography; MR = magnetic resonance; EE = echoendoscopy; EE - FNA = echoendoscopy through fine needle aspiration; RECP = retrograde endoscopic colagiopancreatography

FIGURE 4 – Evaluation of lesion resectability

The initial echoendoscopy was able to detect 96% of the cases of pancreatic mass (23 % of which not seen in the tomography) and was able to perform puncture, leading to a cytological diagnosis of malignancy in more than 95 % of the cases. It presented sensitivity of 93 % and specificity of 100 % in patients with pancreatic mass of suspected tumor, with puncture guided by tomography or cytological brush in the retrograde endoscopic colagiopancreatography. Both results were negative^{14,30}.

Pancreatic neoplasia is more frequent in men, which obtained higher positivity in this study, and in older age. It was therefore suitable to the statistic data found in medical world literature.

Regarding mass size, a recent study of Agarwal et al.² showed increase of resectability of solid pancreatic masses

equal to or smaller than 20 mm (10 in 12 – 83 %), while in masses equal to or bigger than 30 mm, only 7 % (2 in 27). In Brazil, Ardengh et al.³ presented a study with 180 patients having lesions smaller than 3 cm with sensitivity of 82.4 % and specificity of 98.4 %. Hunt and Faigel¹⁷, reviewing four studies including 164 patients presented sensitivity of 91 % and specificity of 100 %. This is much superior to what was found in this study, where approximately 50 % of these lesions were inconclusive to the puncture.

The preferential location was the cephalic portion, also presenting correspondence with the medical literature, what did not favored the positivity, although in a bigger sample this could be presented as a factor of positivity improvement.

In this study it was not possible to characterize the lymph nodes, but it was possible to either detect their presence or not. In medical literature the characteristic description is frequent, and in addition to this their puncture is also carried on, obtaining positivity on average of 90 % and sensitivity of 100 %^{5,6,7,13}.

The simple presence of these lymph nodes in peripancreatic position meant an increase of puncture positivity, what indirectly suggests a more advanced stage. As to obtaining biopsies, it is clear that this influences positivity, that is, when the fragment is obtained, the positivity increases. Ho, et al.²¹ observed the effectiveness of the EE – FNAP in a retrospective study, dividing 10 years of experience with the method into precocious (1996 – 2000) and late (2001 – 2005). As a result, there was an increase of precise diagnosis of 40 % to 95 %, due to the increase in accuracy of cytological diagnosis and mainly due to the increase in obtaining biopsies (microfragments). This is also observed in medical literature. An example of this is when Levy and Wiersema^{21,22} compared two kinds of needles (a 19 gauge Trucut) and the conventional needle. As a surprise a best result was found when the conventional needle was used. This is because the conventional needle is easier to handle especially in a duodenal position. Although the institution where the study was carried on adopts the use of the 22-gauge needle - as described in method -, this was not relevant enough to reflect higher positivity rates. Wittmann et al.³¹ conducted a study associating the two needles and obtained higher sensitivity and specificity. The collection of material to make the blades is important but in this study it presented low performance, which is perhaps explained by the use of the Papanicolau technique and Cell-block, because in Brazil Maluf-Filho et al.²³ presented sensitivity of 95 % and specificity of 100 % using the agar coloring technique.

Anyway, the same kind of pathologic classification of the literature was used, that is, the findings were grouped into categories, not classifying for example the specific kinds of tumors, what permitted the comparison between the findings in several different services⁴. In two cases, the pathology groups put undetermined and inconclusive because they understood that in these two cases the method did not define the pathology in question¹¹. In fact this same author suggests that a new EE – FNAP exam should be made when the results obtained are undetermined or negative, but with high clinical suspicion of cancer, and

presented a study with accuracy of 84 % in this diagnostic confirmation. When this situation of undetermined or negative with strong clinical suspicion of neoplasia persists, despite the image methods such as EE – FNAP, tomography and magnetic resonance are employed, Eloubeidi et al.¹¹ suggests surgical exploration.

Some flaws might be occurring to explain the service's poor performance: low number of punctures, inadequate preparation of material, old fashioned technique employed in the material coloring, absence of pathologist during the procedure, and the experience of the endoscopy professional.

The number of punctures performed may be the main responsible for the positivity's poor performance. LeBlanc, Ciaccia e Al-Assi²⁰ determine a minimum of seven punctures of the lesion and five punctures when there is presence of ganglions, considering that the service does not count on a pathologist during the procedure. Erickson, Sayage-Rabie e Beissner¹³ already called attention to this fact at the first time they researched the influence of the number of punctures performed.

The fact that such materials are collected and prepared by another endoscopist or an intern contributes negatively to a good blade preparation. The preparation of the material using the agar coloring technique presented by Maluf-Filho et al.²³, represented sensitivity of 95 % even with the absence of a pathologist. Eloubeidi et al.¹¹ in their turn refer to the presence of a pathologist during the procedure as compulsory. He is the one who determines the moment to stop collecting material, that is, the pathologist determines if the material is adequate. In a study published in 2003, these authors managed to have sensitivity rates of 98 % and the number of punctures varied from one to 11. The experience of the professional was also evaluated. However, because it considers the basic guidelines established by the American Gastrointestinal Endoscopy Society (ASGE, 2001), even if it is not compulsory in Brazil, it is believed that it was not a relevant factor to the low rate of positivity compared with the one in literature.

Other factors pointed out by Eloubeidi et al.¹² such as co-existence of pancreatitis, technical difficulty of puncture, tumor necrosis, interpathologist variation may lead to flaws in the diagnosis. These flaws show the direction to be followed to improve the service provided. After all, this exam is of utter importance in the diagnosis and in therapeutics, and even nowadays it represents high cost considering the low performance observed if compared to the one demonstrated in medical literature.

CONCLUSIONS

Regarding mass characteristics, when larger is the mass, larger is the positivity of the method; the location didn't correlate with higher positivity; when the lymph nodes were present, there was a tendency to positivity; concerning the number of punctures, the higher number, higher positivity; in relationship to the professional experience in endoscopy, there was no difference in the rate of positivity of the puncture of the solid pancreatic mass.

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RESUMO – Racional - Ecoendoscopia é técnica mista que adiciona as vantagens da endoscopia àquelas da ecografia, somente que o procedimento ecográfico é realizado do interior dos órgãos para fora deles, no sentido centrífugo. **Objetivo** – Verificar a positividade da ecoendoscopia na punção com agulhas (EPTN) ou (EE-PAF) em tumores sólidos pancreáticos baseados na técnica utilizada pelo Serviço de Endoscopia Digestiva do Hospital de Clínicas da Universidade de São Paulo. **Métodos** – Cohorte retrospectiva de 138 pacientes que realizaram ecoendoscopia com punção aspirativa por agulha fina (EE-PAAF) no período de maio de 2004 a junho de 2007. Os dados foram coletados por meio de consulta aos prontuários, constantes do arquivo médico. O critério de inclusão foi a presença de massa pancreática sólida à tomografia computadorizada e o critério de exclusão a presença de tumor pancreático não sólido. Foram utilizadas as seguintes variáveis: característica da massa (tamanho, localização), presença de linfonodo peripancreático, presença de linfonodo em tronco celíaco; número de punções para obtenção de microfragmento; citologia e experiência do profissional executante. O aparelho utilizado foi um ecoendoscópio da marca Olympus, modelo OLYMPUS EUS (EYS) EXERA EU-C60, com transdutor setorial eletrônico e agulhas de 22 gauges da marca Boston Scientific. **Resultados** – Setenta e seis (55,4 %) deles eram do sexo masculino e 61 (44,5 %) do feminino. A idade variou de 16 a 87 anos, com média de 59,9 anos. As lesões foram cefálicas em 94 (68,1 %) dos casos. Massas maiores que 4 cm tiveram percentual de positividade maior, chegando a 40%, mas as lesões menores que 2 cm obtiveram percentual de 43 % de inconclusivo. A obtenção de microfragmentos foi conseguida em 100% dos casos positivos e apenas 73,1 %, quando negativo (P=0,004). Não houve diferença estatística em relação à experiência do endoscopista. Apenas 80 pacientes tiveram anotado o número de punções e notou-se que existe melhor desempenho quanto maior for o número delas. O diagnóstico anatomopatológico definitivo de neoplasia pancreática ocorreu em apenas 41 (29,7 %) indivíduos. **Conclusões** - Em relação às características da massa, quanto maior ela era maior a positividade do método; a localização não correlacionou com maior positividade; há tendência de positividade quando presentes os linfonodos peripancreáticos; em relação ao número de punções, quanto maior o número delas, maior a positividade do método; em relação à experiência do profissional, não houve diferença no índice de positividade da punção da massa pancreática sólida.

DESCRITORES - Massa pancreática sólida. Ecoendoscopia. Punção.

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