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Endoscopic Ultrasound Elastography in the Diagnosis of Pancreatic Cancer

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1. Abstract

Diagnostic assessment of solid pancreatic lesions may represent a real challenge in the clinical practice, even with the aid of tissue sampling by means of Fine-Needle Aspiration (FNA) guided by endoscopic ultrasound. Endoscopic Ultrasonography (EUS) elastography is considered a useful tool for evaluating solid pancreatic lesions. We reported our experience with seven patients with clinical and imaging studies suggestive of solid lesions of the pancreas who underwent endoscopic ultrasound with qualitative elastrography suggestive of pancreatic adenocarcinoma with subsequent histological confirmation of the lesions.

2. Introduction

Pancreatic Ductal Adenocarcinoma (PDAC) is the fourth cause of cancer-related deaths in the United States. Its incidence is on the rise, while mortality rates have remained relatively unchanged. It is forecasted that it will become the second leading cause of cancer-related death within a couple of decades. Overall 5-year survival rate is 6% in the United States. The low survival rate stems mostly from the late stage at which most patients are diagnosed. Only 15-20% of patients are amenable for initial surgical resection [1].

Endoscopic Ultrasound (EUS) is a technology developed in the 1980s and since then it has been established in the clinical practice world-wide. EUS is a beneficial procedure in diagnosis and staging of a wide variety of pathologies of the gastrointestinal (GI) tract. Its development over the years made it possible to obtain tissue samples, perform therapeutic procedures in the gallbladder, drain the common bile duct and pancreatic pseudocysts, and manage pancreatic necrosis [2].

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Elastography (EG) is a non-invasive imaging modality for tissue evaluation, which characterizes mechanical properties such as changes in tissue stiffness and / or elasticity that is also theorized as a possible marker of inflammation, fibrosis, or neoplastic infiltration [3].

Elastography has been investigated by conventional abdominal ultrasound since the early 1990s. EUS Elastography (EUS-EG) was first described in 2005 and is currently a method for the evaluation of pancreaticobiliary diseases [4,5].

The EUS-EG, detects small structural deformations caused by compression and degrees of relative deformation between the region of interest and the rest of the tissues on a scale of 1-255. Each value is assigned a shadow from a tone color spectrum for better visual recognition. Most systems use a red-green-blue color map, in which the stiffer tissue areas are shown in dark blue, while the softer tissue areas are displayed in shades of green to red. The region of interest for elastography evaluation is manually selected and should include the entire lesion (when possible) and also the normal tissue environment. Qualitative analysis includes a score based on a predominant color pattern within the lesion: homogeneously hard, heterogeneously hard, mixed, heterogeneously soft, or homogeneously soft [2, 6-8].

There is a classification with different color patterns to distinguish

malignant from benign masses [9, 10]. Giovannini et al [10] first reported in 2006 a five-score classification based on color patterns of the lesions, with a sensitivity of 100% and a specificity of 67% (Table 1). In this system, lesions with scores between 3 and 5 were considered malignant, while 1 and 2 were considered benign. In 2009 another investigation carried out by the same author [11].

Publishes their results based on a multicenter study using the same scoring system and the precision was 89.2%, and both the sensitivity and the Positive Predictive Value (PPV) were higher than 90%. There is another four-point classification (Table 2) for the diagnosis of pancreatic malignancy with a sensitivity, specificity and general precision of EUS –EG of 100%, 85.5% and 94%, respectively [9].

 Table 1: Five score classification system for endoscopic ultrasound elastography

Score	Color pattern	Stiffness	Histology	Ref.
1.	Green	Homogeneous soft	Normal pancreatic tissue	10;11
2.	Green, yellow and red	Soft heterogenecity	Fibrosis	10;11
3.	Mostly blue with minimal heterogeneity	Hard	Early pancreatic adenocarcinoma	10;11
4.	Central green hypoechoic region and blue tissue outer layer	Hard	Neuroendocrine tumor, metastasis	10;11
5.	Blue lesions with heterogeneity due to necrosis	Hard	Adenocarcinoma de páncreas avanzado	10;11

Score	Color pattern	Stiffness	Histology	
1.	Homogeneous green	Soft	Normal pancreas	9
2.	Heterogeneous, green-predominant	reen-predominant Soft Inflammatory pancreatic masses		9
3.	Heterogeneous, blue-predominant Hard		Pancreatic malignant tumors	9
4.	Homogeneous blue	Hard	Pancreatic neuroendocrine malignant lesions	9

3. Cases Presentation

We retrospectively discuss seven cases of adult patients with clinical manifestations suggestive of malignant lesions of the pancreas, with imaging studies (conventional abdominal ultrasound and Computerized Tomography) that reported solid pancreatic lesions. Four women and three men were studied with a mean age of 65.7 years (range 49-77). All cases underwent endoscopic ultrasound with qualitative elastography and subsequent tissue collection by FNA of the lesion and evaluation by two expert cyto-pathologists. Three cases were sent to Surgery for treatment and the result of the surgical biopsy was taken as histological reference. In the evaluation by endoscopic ultrasound and elastography, all cases had a predominantly blue heterogeneous pattern suggestive of pancreatic adenocarcinoma (Figure 1) which was corroborated by histopathological study. In three patients the tumor lesion was located in the head of the pancreas, another three were in the body and one in the uncinate process of the organ. All solid pancreatic lesions were measured by endoscopic ultrasound with a mean of 40 mm (range 31-56) and they were staged using the TNM system [12] and in four of them they presented invasion of vascular structures. All the variables studied are shown in (Table 3).

Dationt	Gender	Age	Pancreas	Size of the	Cancer	Vascular
ratient		(years)	mass location	mass(mms)	Staging	invasion
1	Female	68	Head	32	T2N1M0	
2	Female	64	Uncinate	49	T4 N2 M0	CAH
3	Male	49	Head	31	T2N2M0	
4	Male	77	Body	33	T2 N1M0	SMA
5	Female	66	Head	42	T3N0M0	
6	Female	77	Body	48	T4N2M0	SV
7	Male	59	Body	56	T4N2 M0	SMA

Table 3: Characteristics of the patients studied

*CHA, common hepatic artery; SMA, superior mesenteric artery; SV, splenic vein



Figure 1: Images of pancreatic lesion obtained by endoscopic ultrasound with elastography. A: Image of a solid pancreatic lesion. B: Elastographic image of a solid pancreatic lesion showing a predominant blue heterogeneous pattern, suggestive of pancreatic adenocarcinoma.

5. Discussion

EUS can provide detailed, high-resolution images of the pancreas. However, the specificity of EUS images for the diagnosis of pancreatic masses is low (50–60%). Ultrasound elastography is a relatively new diagnostic technique for measuring tissue elasticity (hardness). It is mainly used for distinguishing between malignant and benign tumors of the mammary gland, thyroid, prostat, liver and pancreas. It is also used for evaluating hepatic and pancreatic fibrosis and has a significant influence on clinical decision making. There are various types of elastography devices, and each utilizes different mechanisms. In the Japanese guideline on ultrasound elastography, the various types of elastography are classified into strain elastography, shear wave elastography, transient elastography, and Acoustic Radiation Force Impulse (ARFI) imaging [13].

In a study carried out by Facciorusso A et al. [14] where 54 patients with solid lesions of the pancreas were evaluated. The median age was 68 years and 64.8% of patients were male. The majority of lesions were located in the pancreatic head or uncinate (62.9%) and the median size was 35 mm. About one fifth of the whole population (20.3%) finally underwent surgery and the diagnosis of adenocarcinoma was confirmed from a surgical specimen or by the patient's clinical course in 85.1% of cases. Another study conducted by Altonbary AY et al [15] with 116 patients (97 with malignant lesions and 19 with benign lesions). There were 69 men and 47 women. Their median age was 55.9 years (range, 12–78 years). Most of lesions were located in the pancreatic head (51.5%) with the median size 40mm and final histological diagnosis were adenocarcinoma in the 80.4% of all cases.

In a meta-analysis carried out by Li X and collaborators [16] where 10 studies were analyzed and 781 patients participated, various types of endoscopic ultrasound elastrography were evaluated. In the studies that used the color pattern as the diagnostic standard, the pooled sensitivity, specificity, positive Likelihood Ratio (LR), negative LR, and diagnostic OR (Odds ratio); were 0.99 (0.97-1.00), 0.76 (0.67-0.83), 3.36 (2.39-4.72), 0.03 (0.01-0.07) and 129.96 (47.02-359.16), respectively in the evaluation of the differentiation between inflammatory lesions and adenocarcinoma of the pancreas. Another meta-analysis [17] where 225 articles were evaluated about the diagnostic utility of EUS-EG in the diagnosis of pancreatic masses, in relation to qualitative methods the pooled sensitivity (random-effect model) and specificity (random-effect model) were 0.97 (95%CI, 0.95-0.99) and 0.67 (95%CI, 0.59-0.74,), respectively, and concludes that EUS-EG is reliable and promising for distinguishing malignant from benign solid pancreatic masses with a high sensitivity.

Another study carried out by Okasha H [18] where 172 patients with solid lesions of the pancreas were evaluated, most of the lesions were located in the head of the pancreas (118) and 123 of them were malignant tumors. In the analysis of qualitative elastog-

raphy based on color patterns had a sensitivity of 99%, specificity of 63%, positive predictive value (PPV) of 87%, Negative Predictive Value (NPV) of 96%, and accuracy of 88%.

One study where determinates the potential of endoscopic ultrasound elastography in determining the stage of pancreatic tumor, were includes 81 patients with malignant pancreatic lesion in different clarified stages. The mean age of patients was 60.11±13.57 vears. With regard to staging based on tumor size (T staging), most patients were observed to be in the T4 stage (60.5%), and only 3.7% of the participants were categorized in the T1 stage. The findings regarding number and location of the involved lymph nodes showed that 77.8% of participants belonged to the N0 stage. M staging revealed metastasis to other organs. Most patients were diagnosed with M0 stage (75.3%), and 24.7% of them were staged as M1. Elastography could not significantly discriminate T stage, N stage, or M stage of tumors (p=0.57, p=0.92, p=0.11, respectively). Moreover, the Spearman rank correlation coefficients for the correlation between T staging, N staging, M staging and semiquantitative elastography were not significant (p=0.40, p=0.94, p=0.39, respectively) [19].

In the study carried out by Fujii Y et al. [20] for the 31 tumors located in the pancreatic head, they evaluated 15 SMVs (Superior Mesenteric Vein), 16 Portal Veins, and 31 SMAs (Superior Mesenteric Artery). Similarly, for the 26 tumors located in the pancreatic body or tail, we evaluated 26 SPVs (Splenic Vein) and 26 SPAs (Splenic artery). They evaluated the diagnostic abilities for the major veins (SMV, PV, and SPV) and arteries (SMA and SPA). The sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and accuracy of EUS diagnosis were 89% (16/18), 92% (36/39), 84% (16/19), 95% (36/38), and 91% (52/57), respectively, for the major veins and 83% (5/6), 94% (48/51), 63% (5/8), 98% (48/49), and 93% (53/57), respectively, for the major arteries.

6. Conclusion

EUS plays an important role in the evaluation of pancreatic masses and in determination of the accurate stage of pancreatic cancers by providing cytological and histological confirmation. Also is a highly useful tool to detect vascular invasion in patients with pancreatic cancer and the elastography is reliable and promising tool for distinguishing malignant from benign solid pancreatic masses with a high sensitivity.

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