THE ROLE OF ENDOSCOPIC ULTRASOUND ELASTOGRAPHY IN DIAGNOSIS OF PANCREATIC LESIONS

Thesis

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List of Abbreviations

Abbreviations	Meaning
ANP	Acute necrotizing pancreatitis
BI-RADS	Breast imaging reporting and data system
CBDD	Common bile duct dilation
DCIS	Ductal carcinoma in situ
EUS	Endoscopic ultrasound
EUSE	Endoscopic ultrasound elastography
EUS-FNA	EUS fine needle aspiration
PA	Pancreatic abscess
PDD	Pancreatic duct dilatation
PNETS	Pancreatic Neuroendocrine tumors
MRCP	Magnetic resonance cholangio pancreatography
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
ROI	Region of interest
TBN	Trucut biopsy needle

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Abstract

Thirty patients underwent EUS examination with elastography for evaluation of pancreatic masses. They were 22 males and 8 females with a mean age of 54±8.6 years. The final histological assessment was based on the FNA, surgical and endoscopic biopsy results. Eleven cases were diagnosed by FNA, 5 cases were diagnosed by surgical exploration and pathological results, 4 cases were diagnosed by following up the size of masses. In 5 cases, major vessels were found to be involved. Two cases were having distant metastasis, and three cases were diagnosed with endoscopic biopsy. The final diagnosis of the pancreatic masses included pancreatic malignant masses (n = 25), pancreatitis (n = 2), papillary adenoma (n = 2) and papillary carcinoma (n =1). The elastographic images were interpreted as benign (score 1 + 2) in 2 cases, score 3 in 6 cases and malignant (score 4 + 5) in 22 cases. Considering score 3 as benign, the calculated sensitivity, specificity, positive and negative predictive values were: 88%, 80%, 95.6% and 57.14% respectively, with a global accuracy of this new technology of 89.2%. Considering score 3 as malignant, the calculated sensitivity, specificity, positive and negative predictive values of EUS elastography were 100%, 40%, 89.28% and 100 respectively.

EUS correctly diagnosed 23 cases with malignant pancreatic lesions while one case diagnosed as malignant was finally proved benign. EUS also correctly diagnosed 4 benign cases. Two cases were indeterminate on EUS diagnosis, one was proved to be benign and one was proved to be malignant on final diagnosis.

The calculated sensitivity, specificity, positive predictive value, negative predictive value and accuracy of EUS in diagnosing pancreatic masses were 95.8%, 83.3%, 95.8%, 83.3%, 90% and 90% respectively

when the indeterminate cases were considered as benign. On the other hand, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 100%, 66.6%, 92.3%, 100% and 93.3% respectively when the indeterminate cases were considered as malignant.

When adding tissue elastography to EUS diagnosis, the sensitivity, specificity, positive predictive value, negative predictive and accuracy improved to become 100%, 80%, 96.2%, 100% and 96.7% respectively.

INTRODUCTION

Elastography has recently been presented as a novel technique that can be applied during ultrasound (US) examination to assess and measure tissue elasticity. Knowing that malignant tissues are generally harder than normal surrounding tissue, elastography might provide interesting clinical information to help distinguish benign from malignant tissue based on their specific tissue consistency ***(Fritscher-Ravens A et al 2002)***.

Clinical research has shown promising results in differentiating benign from malignant tissue in the thyroid gland, breast, prostate and to assess liver fibrosis ***(Lyshchik et al 2005)***. Recently, elastography has also been introduced during EUS examination to examine different organs ***(Giovannini,.et al 2006)***.

Our study is a continuation of previous Researches to validate the potential role of elastography in distinguishing benign from malignant pancreatic focal lesions.

AIM OF THE STUDY

The aim of this study is to evaluate the role of the newly introduced technique of EUS elastography in differentiating benign from malignant pancreatic lesions and its role in the routine work up of pancreatic masses.

ANATOMY OF THE PANCREAS

An understanding of pancreatic anatomy is important in delineating the cross-sectional anatomy of the pancreas and the causation of pain in pancreatic disease. The pancreas varies in shape and lies in the anterior pararenal space. The head of the pancreas lies within the curve of the duodenal loop, and the inferior vena cava and right renal vessels lie posteriorly. The common bile duct receives the main pancreatic duct as it passes through the pancreatic head and then drains into the duodenum at the ampulla ***(Hammel et al., 2008).***

The gastroduodenal artery may be seen anteriorly at the pancreatic head and neck. The head of the pancreas is the most bulbous part of the gland, which then narrows to the neck. The union of the superior mesenteric and splenic veins, which forms the portal vein posteriorly, marks the anatomic position of the pancreatic neck. The pylorus lies anteriorly. The lesser sac lies anterior to the pancreas, whereas the splenic vein runs along its posterosuperior surface. The tail of the pancreas is related to the spleen, left adrenal gland, and upper pole of the left kidney ***(Henry G et al.,2003).***

Sonograms of the pancreas typically demonstrate a homogeneous echo pattern, and the pancreas is more echogenic than the liver. The pancreatic head measures 2.5 width and 3.5cm length ; the body, 1.75 width and 2.5cm length ; and the tail, 1.5 width and 3.5 cm length . The size of the pancreas varies considerably; therefore, reliance on size alone can lead to diagnostic errors.

Generally, the size of the gland decreases with patient age, while echogenicity increases. The pancreas is more echogenic than the liver in 52% of young adults and equally echogenic in 48%. With the use of modern ultrasonographic machines, the main pancreatic duct can be identified in 85% of patients. On sonograms, the normal duct diameter is 1.3mm ± 0.3. In patients with gallstones, the average diameter is 1.4mm. ***(Kim et al., 2008).***

The typical criteria for pancreatic size on CT scans are the following: the head is 23mm; neck, 19mm; body, 20mm; and tail, 15 mm. By using optimal CT techniques, the pancreatic duct can be identified in just more than 50% of the patients. Normally, the pancreatic diameters demonstrated on CT scans vary from 2-4mm, but the effect of pixel averaging on normal pancreatic duct measurements is significant and can make such measurements unreliable. Errors of 1 or 2mm may occur***(Kim et al., 2008).***.

In most patients, a normal pancreatic duct is seen on images obtained with MRI sequences and magnetic resonance cholangiopancr-eatography (MRCP) ***(Ali Nawaz 2009)***

NEOPLASMS OF THE PANCREAS

Neoplasms of the endocrine pancreas can be divided into functional and nonfunctional varieties. Most pancreatic endocrine neoplasms discovered clinically are functional; ie, they secrete one or more hormonal products into the blood, which leads to a recognizable clinical syndrome.

In 1927, ***Wilder et al*** described the first hormone-producing pancreatic tumor syndrome in a patient with hypoglycemia and a metastatic islet cell tumor, extracts of which caused hypoglycemia. Subsequent to this initial description of insulinoma syndrome, other classic pancreatic endocrine tumor syndromes have been described. The first is Zollinger-Ellison syndrome (also termed gastrinoma syndrome), described by Zollinger and Ellison .,et al in 1955**.** The second comprises a group of 3 tumor syndromes, termed Verner-Morrison syndrome, WDHA (watery diarrhea, hypokalemia, and achlorhydria) syndrome, and pancreatic cholera (also termed vasoactive intestinal peptide [VIP]–releasing tumor or VIPoma) and were described by Verner and Morrison in 1958. The third is glucagonoma syndrome, described by Mallinson et al in 1974. The fourth is somatostatinoma secreting somatostatin ***(Ganda et al., 1977).***

Several other rare clinical syndromes have been proposed as possible functional endocrine syndromes associated with pancreatic neoplasms. These include calcitoninoma described by ***(Howard A 1989; and McLeod 1992)*** parathyrinoma, growth hormone-releasing factor–secreting tumor (GRFoma), adrenocorticotropin

hormone–secreting tumor (ACTHoma), and neurotensinoma ***(Meko et al., 1994).***

Patients with pancreatic neoplasms that have the histologic characteristics of a pancreatic endocrine tumor but no associated elevation in plasma hormone levels, excluding the pancreatic polypeptide level and those without a recognizable clinical syndrome are considered to have nonfunctional pancreatic endocrine tumors. A subset of patients with nonfunctional pancreatic endocrine neoplasms, the tumor secrete pancreatic polypeptide (ie, PPomas). Pancreatic polypeptide (PP) is a product that appears to be a marker for pancreatic endocrine tumors, but it is not a mediator of any specific PP-related clinical syndrome ***(Langstein et al., 1990).*** Other nonfunctional pancreatic endocrine tumors likely secrete unknown products that are of little or no clinical significance.

Patients with functional pancreatic endocrine neoplasms have physiologic derangements related to the normal action of the hormonal product that the tumors overproduce. Thus, patients with an insulin-secreting tumor (ie, insulinoma) have pathophysiologic findings of hypoglycemia; patients with a gastrin-secreting tumor (ie, gastrinoma) have hypersecretion of gastric acid, which often leads to the development of peptic ulcers (ie, Zollinger-Ellison syndrome); and so on. In contrast, patients with nonfunctional pancreatic endocrine neoplasms typically present later in the course of their disease, when their tumors begin to cause symptoms related to a mass ***(Ganda et al., 1977).***

Frequency

Neoplasms of the endocrine pancreas occur in 2 distinct epidemiologic groups. Sporadic form, which develops in patients without a significant personal or family history of endocrine disorders. The second form affects kindreds with the multiple endocrine neoplasia type 1 (MEN 1) syndrome in a pattern of autosomal dominant inheritance ***(Norton et al., 1993).*** Approximately 80% of individuals with MEN 1 syndrome have one or more pancreatic neoplasms in their lifetime; gastrinoma and insulinoma are the most commonly identified lesions ***(Helmrath et al., 1997).***

Clinically recognized neoplasms of the endocrine pancreas are rare, with an overall annual incidence in the United States of 3-10 cases per million persons ***(Buchanan 1986 ;and Eriksson 1998).*** However, the much higher prevalence of these tumors in unselected autopsy specimens, i.e, 0.5-1.5%, reflects the indolent nature of many of these tumors ***(Jenssen et al., 2002).***

Insulinomas and gastrinomas occur with roughly equal annual incidences; together they account for more than half of all clinically apparent pancreatic endocrine tumors ***(Jensen et al., 1998)***. VIPomas are one-eighth and glucagonomas are one-seventeenth as common, whereas somatostatinomas are even rarer**.** Nonfunctional tumors account for 14-48% of all recognized neoplasms of the endocrine pancreas ***(Eriksson et al., 1995).***

Mortality/Morbidity