REVIEW ARTICLE

Somatostatin in Treatment of Acute Recurrent Pancreatitis and Role of Endoscopic Ultrasonography in The Diagnostic Workup

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ABSTRACT

The pancreas is an elongated, soft, flat, lobulated, and yellowish gland located on the posterior abdominal wall in a transverse orientation. The structure is located in the retroperitoneum and has a thin capsule. An abrupt response to pancreatic injury is known as acute pancreatitis (AP). Chronic pancreatitis can lead to enduring harm to the composition and the pancreas' endocrine and exocrine functions. The term idiopathic RAP (IRAP) is employed when the reason cannot be readily identified by the assessment of physical examination, medical history, basic laboratory tests (calcium and serum triglyceride levels, for example), and diagnostic imaging studies (e.g., CT scans and transabdominal ultrasounds). With endoscopic ultrasonography (EUS), you may see the inside of your digestive tract and any surrounding tissues in high resolution and real time. When it comes to evaluating a wide variety of benign and malignant GI illnesses, this technique is both efficient and cost-effective. Somatostatin inhibits the release and manufacture of certain enzymes, which in turn decreases the pancreas' ability to absorb amino acids. The release of somatostatin from the pancreatic islets is stimulated by high glucose concentration.

Keywords: Somatostatin. Endoscopic Ultrasonography, Recurrent idiopathic acute pancreatitis, Gastrointestinal stromal tumors (GISTS)

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INTRODUCTION

Approximately 275,000 hospital admissions occur each year due to AP. The majority of individuals hospitalized with pancreatitis typically experience a minor form of the condition and can be released within a few days. Around two percent of those who get AP will die from it. Depending on the root cause of pancreatitis, the rate of recurrence of AP might be anywhere from 0.6 percent to 5.6 percent. Pancreatitis caused by alcohol intake is associated with a higher recurrence rate. **(1)**.

Chronic pancreatitis is caused by alcohol consumption more often than any other substance. One of the major risk factors is smoking. Tropical pancreatitis, idiopathic pancreatitis, injuries, cystic fibrosis gene mutations, hereditary pancreatitis, ductal blockage (pancreas divisum, tumors, stones, pseudocysts, and trauma), and systemic disorders like systemic lupus erythematosus are among the other potential causes **(2).**

"Two or more episodes of AP" is what makes an episode RAP. The following reasonable conditions have been added to this fundamental definition: the symptoms must completely disappear between attacks, there must be no imaging alterations that indicate CP, and there must be a minimum of three months among the first episode and any subsequent ones **(3)**.

EUS has become an increasingly prevalent adjunct to or substitute for conventional surgical treatments. Since the 1980s, when it was predominantly employed for diagnostic purposes, EUS has evolved into an increasingly utilized therapeutic modality. Therapeutic EUS-guided therapies have been steadily improving due to the substantial levels of technical and clinical efficacy that have been documented. In recent years, endovascular ultrasound (EUS) has found use in a variety of novel procedures, including the following: port vein (PV) sampling, angio-therapy, a biopsy of the liver, the gallbladder drainage, gastro-jejunostomy creation, contrast-

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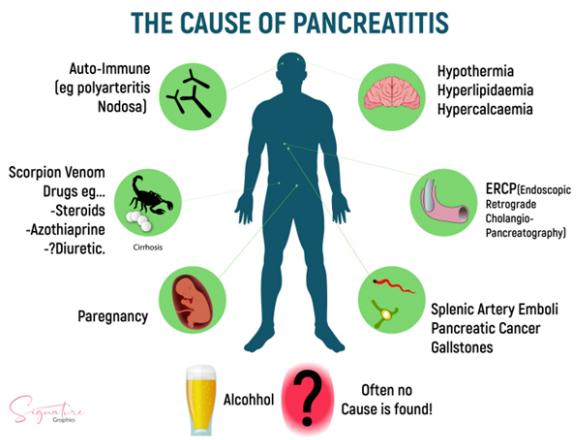

Figure 1: This is a graphic illustration of the causes of AP. Contributed by Dr Amina Tariq **(7).**

enhanced harmonies EUS, liver biopsy, and endovascular retrograde cholangiopancreatography (ERCP) for patients with surgically altered anatomy. This exciting and dynamic technology is ripe with innovative advancements. **(4)**.

EUS is an imaging technique that integrates high frequency ultrasound with endoscopic visualization to provide visual representation of the gastrointestinal (GI) tract wall and adjacent organs and blood vessels. Locating specific lymph nodes and understanding the histological analogues of the five GI tract wall layers are the cornerstones of most EUS methods. **(5)**.

The objective of this prospective research was to assess the role of EUS after the first episode of IAP for identification of possible causes for AP when other investigative methods as TAUS and contrast CT scan fail.

Pancreatitis

Etiology

Individuals without gallstones or a history of severe alcohol consumption should have their triglyceride levels evaluated, fresh guidelines put forward by the American College of Gastroenterology stipulate. According to their recommendation, this should be taken into account if the concentration is more than 1000 mg/dl. Also, according to the guidelines, pancreatitis in those over the age of 40 is more likely caused by a tumor in the pancreas. Also, It may be worth considering genetic testing for individuals under the age of Thirty who have a verified family record of pancreatic illness and have no other recognized causes of pancreatitis. **(6)**.

The occurrence rate of chronic pancreatitis varies from five to twelve cases per 100,000 individuals per year. Fifty instances out of every 100,000 people are reported to have chronic pancreatitis. It is most prevalent between the ages of 30 and 40, and males are affected at a higher rate than females **(7)**.

Pathophysiology

Chronic pancreatitis can develop after a series of acute attacks, pancreatic fibrosis and infiltration of inflammatory cells are the end outcome. As a result, pancreatic insufficiency develops over time. **(2)**.

Genetics of Pancreatitis

Digestive proteases, a trypsin the inhibitor, and other proteins highly expressed in the pancreas are represented by the majority of risks for pancreatitis. The many mutations and genetic alterations that cause pancreatitis were classified into pathogenic pathways based on the functional research. **(8)**.

Systemic inflammation's function in pancreatitis

The first stage of inflammation is NFκB activation.

As soon as pancreatitis begins, throughout the first few minutes of the illness, the nuclear factor kappa- light-chain enhancer of B cells that have been activated (NFκB) begins to activate. The main function of NFκB is to control the expression of genes that are part of the immune response. The quick activation of NFκB during the start of pancreatitis is explained by its presence in the cytoplasm. **(9)**.

History and physical examination

Discomfort in the epigastric region that travels to the back is a hallmark of AP. Symptoms such as nausea, vomiting, and severe pain are common descriptions (2).

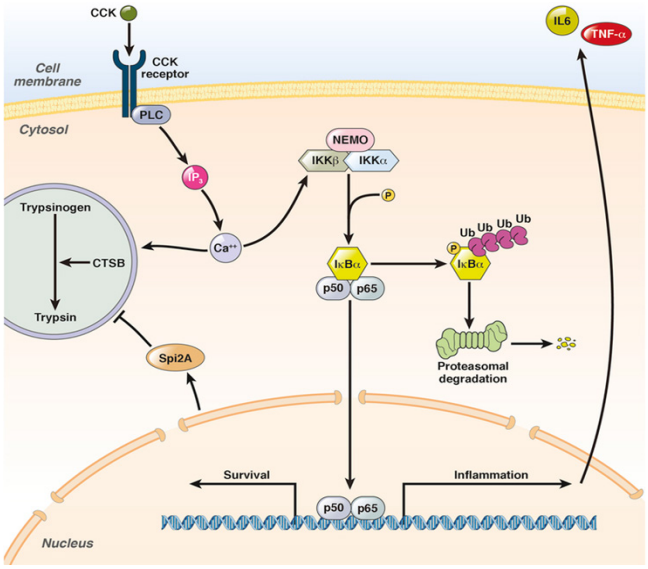

Figure 2: Members of the NFκB pathway include pancreatic acinar cells. In the early phases of its development, NFκB activation is comparable to trypsinogen activation. On the other hand, NFκB does not require trypsinogen activation in order to become active. Both are triggered by cytoplasmic Ca2+ influx. At the same time as protease activation takes place, phosphorylation of IκBα, proteasomal degradation and NFκB (p65/p50) translocation to the nucleus take place and occur simultaneously. Through its role as a transcription factor, NFκB is responsible for facilitating two distinct types of gene transcription: pro-inflammatory (such as IL6 or TNFα) genes that initiate the immune response, and pro-survival genes. In order to protect cells, NFκB has the ability to directly influence protease activity through the process of up-regulating Spi2A, which is a serine protease inhibitor **(8).**

Diagnosis

Histopathology

Histopathological assessments of AP are based on the degree of sickness, particularly the presence or absence of necrosis. We can categorize the illness as follows: A pancreatitis that is hemorrhagic and necrotizing, as well as an interstitial pancreatitis, are two possible conditions.

Edema, necrosis, and surrounding fat stranding of the pancreas are possible complications of AP. There is just a little amount of fat necrosis in mild pancreatitis, but in severe cases, large areas of fat necrosis have fused. This is related to parenchymal damage and localized hemorrhages. **(2)**.

Differential diagnosis

Other possible reasons of epigastric stomach discomfort besides AP include (2) cholecystitis and peptic ulcer disease (PUD), Acute Mesenteric Ischemia, Perforated viscus, Choledocholithiasis and Intestinal obstruction. Chronic pancreatitis can have other causes, such as acute recurrent pancreatitis, malignancy of the pancreas, or chronic mesenteric ischemia.

Treatment

Adequate fluid resuscitation is the first line of defense against AP. According to the latest recommendations, this should be administered intravenously as a bolus of 20 ml/kg of Lactate Ringer's (LR) followed by three ml/kg per hour **(6)**.

Urgent ERCP within 24 hours after diagnosis is advised for those with AP and acute cholangitis, in addition to a GI consultation. It is possible to do a cholecystectomy on people who have gallstones within the gallbladder on the same hospitalization. Nevertheless, surgery might be postponed until the inflammation in the area has diminished if necrotizing AP is a concern **(2)**.

Pain management, smoking and alcohol cessation counseling, and pancreatic enzyme replacement are all part of the treatment plan for chronic pancreatitis. A low-fat diet consisting of many short meals should be the primary recommendation for patients. Extracorporeal shock wave lithotripsy (ESWL) for duct stones, celiac plexus blocks, or surgery may be suggested to individuals whose medicinal therapies have not been successful **(2).**

Prognosis

AP is associated with a 2% mortality rate. Endocrine and exocrine insufficiency can occur in around twenty percent to thirty percent of individuals after an episode of AP **(1)**.

Complications

AP complications can be categorized as either systemic or local. However, a pseudocyst and walled-off necrosis usually appear more than four weeks following the beginning of AP, and peripancreatic fluid collections typically appear within that time frame. The updated Atlanta requirements have led to the following local complications **(2)**: Pancreatic pseudocyst(> four weeks), Peri-pancreatic fluid collection(early phase), Walled-off necrosis (> four weeks) and Acute necrotic collection(< 4 weeks).

The following are examples of systemic complications: ARDS, Compartment syndrome, AKI, and DIC.

Pseudoaneurysms, diabetes, splenic vein thrombosis, recurrent AP, and the risk of pancreatic cancer development are some of the problems that can arise from chronic pancreatitis.

Epidemiology

Idiopathic pancreatitis and other causes of pancreatitis do not always have their results published. Idiopathic cases, in contrast to those with biliary causes, have been found to have greater rates of recurrence and progression, according to some research **(7)**.

Causes

Toxic and metabolic, genetic, autoimmune, and obstructive pathways are some of the shared causes among RAP & CP. The sections that follow will focus on a number of causes that are of special interest to endoscopists **(10)**.

Biliary microlithiasis

Patients with an intact gallbladder who are at increased risk for biliary microlithiasis, an IRAP, due to circumstances Those who have experienced things like pregnancy, serious illness, sudden weight loss, prolonged fasting, using ceftriaxone or octreotide, undergoing a bone marrow or organ transplant, and so on are at a higher risk of developing this disease. In microlithiasis, little gallstones (< 3 mm) are present, which are not easily detectable on transabdominal ultrasonography (TAUS), but have the potential to traverse the cystic duct and impact the ampulla of Vater. A heightened vulnerability to obstructive AP episodes can develop from ampullary stenosis, which can be caused by an inflammation and fibrosis cycle brought on by the repeated passage of tiny stones. Despite microlithiasis's "invisible" status on TAUS, it can coexist with biliary sludge, which is more discernible on endoscopic ultrasonography (EUS), repeat TAUS, and other types of TAUS **(11)**.

Pancreas divisum

Pancreas divisum (PD) is a frequent congenital anomaly that may cause obstructive pancreatitis by blocking the pancreatic duct's outflow. Two distinct sprouts, the ventral and dorsal buds, give rise to the pancreas, and they each exit the foregut via their own duct. As the first trimester progresses, the ventral bud joins with the dorsal half and rotates axially. In most cases, the pancreas drains itself twice as efficiently via the ventral and dorsal channels, with the help of the major and minor papillae. When a person has PD, it's because their ductal systems don't fuse properly, so their dorsal and ventral ducts drain separately, or because they only fuse partially, leaving a thread-like connection between the two **(12)**.

Endoscopic PD treatment includes a tiny papillotomy to promote dorsal duct drainage. After a little papillotomy, we often place a temporary pancreas stent to avoid post-ERCP pancreatitis and maintain the orifice open while the patient heals. Possible complications include dorsal duct cannulation and minor papilla implantation. To the right of the main

papilla lies the minor papilla, which is often easiest to see with a magnification lens. Sometimes the minor papilla is a mound or "mini-papilla"; sometimes it is flat with an almost imperceptible aperture. The hole may open after intravenous secretin infusion stimulates pancreatic juice production. The surrounding mucosa can benefit from methylene blue spray **(13)**.

Sphincter of Oddi Disorders

In individuals who have had cholecystectomy, IRAP may occasionally be attributed to abnormalities of the sphincter of Oddi (SODs). Pancreatic SOD is a part of the famous Milwaukee classification; most people with IRAP fall under type 2 (pancreatic pain, recurrent elevations in amylase or lipase, and normal pancreatic duct) **(12)**.

Few randomized trials have defined the best endoscopic procedure and intervention effectiveness for SOD, and previous methods have been inconsistent. Additionally, many trials had insufficient follow-up, and the effects of endoscopic treatment for IRAP have been poorly described in the majority of research. Due to the time and danger involved, as well as the lack of precision in sphincter of Oddi manometry (SOM) measurements, empiric sphincterotomy without manometry has been frequently utilized in RAP **(14)**.

During follow-up, there was no distinction in the rate of RAP (48.5% versus 47.2%, p = 0.20). In comparison to pancreatic SOD retrospective studies, the rates of RAP following both EBS/EDS were much higher **(15)**.

Ampullary and Pancreatic Neoplasms

Individuals with RAP, People over the age of 40 who have acquired the illness recently, in particular, should be continuously examined for the possibility of a malignancy. AP episodes may occur when the pancreatic duct becomes blocked due to duodenal, ampulla, or pancreatic cancer. **(16)**.

Pancreatitis presumably has its origins in the pathophysiology of mucous production causing ductal obstruction. Compared to patients without AP, those with IPMN who experience it at an earlier age are more likely to develop cancer. Although branch-duct IPMN can also detect AP, it is more common in main-duct and mixed-type variants. Confirming that the cyst is the source of pancreatitis might be challenging due to the high prevalence of unintentional IPMNs in situations with branch-duct IPMN **(12)**.

Autoimmune Pancreatitis

In type 1 autoimmune pancreatitis (AIP), it is rather uncommon to observe the presence of RAP. Instead, more frequently observed presentations include obstructive jaundice, diabetes, and weight loss. When AP occurs, the probable explanation is stricturing of the pancreatic duct. Based on a comprehensive analysis of nine studies published in 2008, involving a total of 140 patients diagnosed with acute intermittent porphyria (AIP), Pancreatitis or recurrent pain was observed to be a significant occurrence, as was observed by the researchers. In total, 10.1% of the participants were determined to be experiencing pancreatitis or recurring discomfort. The prevalence of RAP

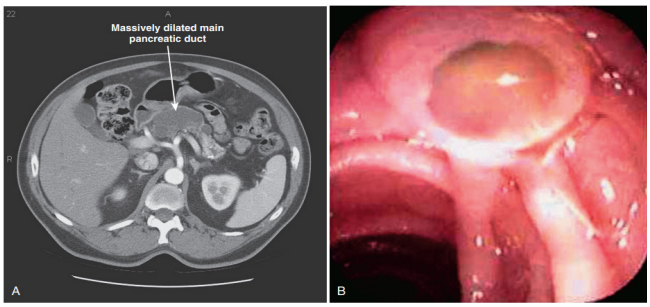

Figure 3: If an intraductal papillary mucinous neoplasm (IPMN) is found in the main duct gland, the patient will be diagnosed with recurrent acute pancreatitis (RAP). A CT scan reveals that the pancreatic duct has been significantly enlarged. The sideviewing endoscopy allows for the discovery of a gaping papilla that is accompanied by mucus extrusion. (2)

seems to be higher in the type 2 histological variety compared to the type 1 version. The study's conclusions are in agreement with this. Diagnosing type 2 AIP is more difficult than type 1 AIP due to the lack of a serological indication and the increased difficulty in obtaining definitive histology. **(17)**.

Choledochocele

Choledochoceles are cystic dilations that may develop in the intraduodenal segment of the common bile duct (CBD). These dilations manifest as an aberrant expansion of the duodenal CBD. They belong to the rarest kind of choledochal cysts, type 3. Most people with symptomatic choledochoceles will have

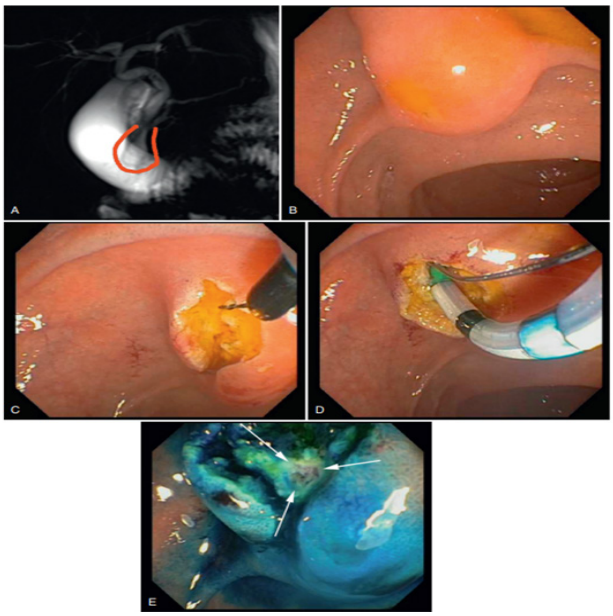

Figure 4: Diagnosis and treatment of choledochocele using endoscopic methods. An 8-year-old child experienced idiopathic acute recurring pancreatitis. An enhanced MRCP reveals a large saccular choledochocele with distinct entrances for the common bile and pancreatic ducts (highlighted in red). Image showing a notable choledochocele as seen through an endoscope. Endoscopic therapy involved procedures such as needle-knife lumen unroofing and biliary cannulation and sphincterotomy extension. During the procedure, the pancreatic sphincter was safely exposed using secretin injection and methylene blue spray, as shown by the arrows. (12).

recurrent abdominal pain (RAP). The bile ducts backing up into the pancreas is a common cause of this illness. Although very few cases have been documented, the likelihood of cancer developing from choledochoceles is thought to be much lower than from other types of choledochal cysts. When treating choledochoceles, EBS is now considered the gold standard (18).

Diagnostic work up of pancreatitis

Three phases can be used to assess and treat RAP. A thorough history, laboratory testing, ultrasonography (with or without CT imaging), and study of attack records are all part of the main evaluation that aims to identify simple and obvious causes. In the second round of testing, doctors employ advanced imaging and lab work to uncover any "occult" biliary, structural, or genetic issues. Endoscopic diagnostics, as well as empiric endoscopic or surgical procedures, may be recommended during the tertiary evaluation to determine the causes or to prevent attacks. Although AP first examinations are typically conducted while patients are hospitalized, Secondary and tertiary assessments are commonly performed in outpatient clinics. Several interdisciplinary "Pancreas Centers of Excellence" were created across the country to provide comprehensive evaluations for individuals suffering from complex pancreatic diseases like IRAP. **(19)**.

Endoscopic Ultrasound

EUS is commonly utilized in the secondary assessment of IRAP and can assist in directing further evaluation and treatment. The imaging technique is comparable to MRCP in its ability to provide detailed visualization of the pancreas. The advantages of this procedure compared to MRCP are luminal visualization, improved detection of biliary sludge and stones, the ability to collect tissue and fluid samples, and the capability to identify parenchymal changes that suggest chronic pancreatitis. Based on current medical evidence, it is possible that EUS may have certain advantages over CT when it comes to identifying small masses **(20)**.

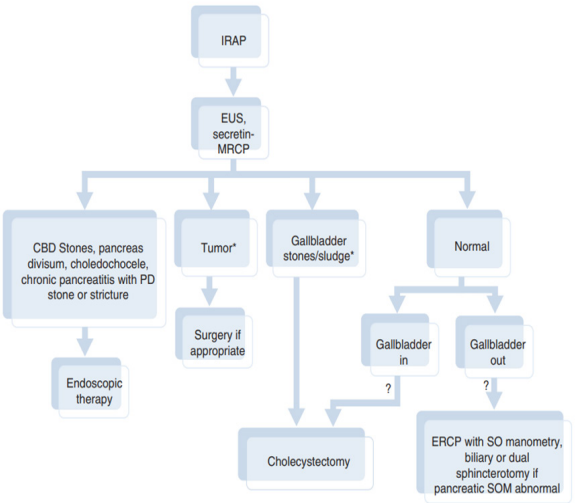

Figure 5: Undetected recurrent pancreatitis treatment algorithm. Indicates conditions where EUS outperforms MRCP in diagnosis. (12).

Endoscopic Ultrasound

With EUS, the GI tract and its surrounding extramural structures can be seen in real-time with great resolution. It is an economical, quick, and accurate way to diagnose a variety of GI disorders, both benign and malignant **(21)**.

Equipment, Devices, and Techniques

In order to capture ultrasonic images, a linear echoendoscope utilizes the sagittal plane, which is perpendicular to its long axis. A diagnostic and staging examination is conducted using the radial echoendoscope. The device offers a comprehensive view of the esophagus, rectum, duodenum, stomach, and surrounding structures of the gastrointestinal tract with its 360-degree field of view (21).

EUS-guided fine-needle aspiration (FNA) is a technique used to identify and collect fluid collections or solid lesions in close proximity to the gastrointestinal tract.

(21).

EUS-guided fine-needle biopsy (EUS-FNB) involves the use of EUS to detect and collect samples from solid lesions that are near the gastrointestinal tract **(22)**.

Indications for EUS

There are different categories for EUS indications, including therapeutic EUS, evaluation of subepithelial deviations, evaluation of extraluminal anomalies and staging of gastrointestinal malignancies.

Staging of GI cancers

To select the most suitable treatment for a patient with upper GI malignancy, precise staging is vital. EUS has become an

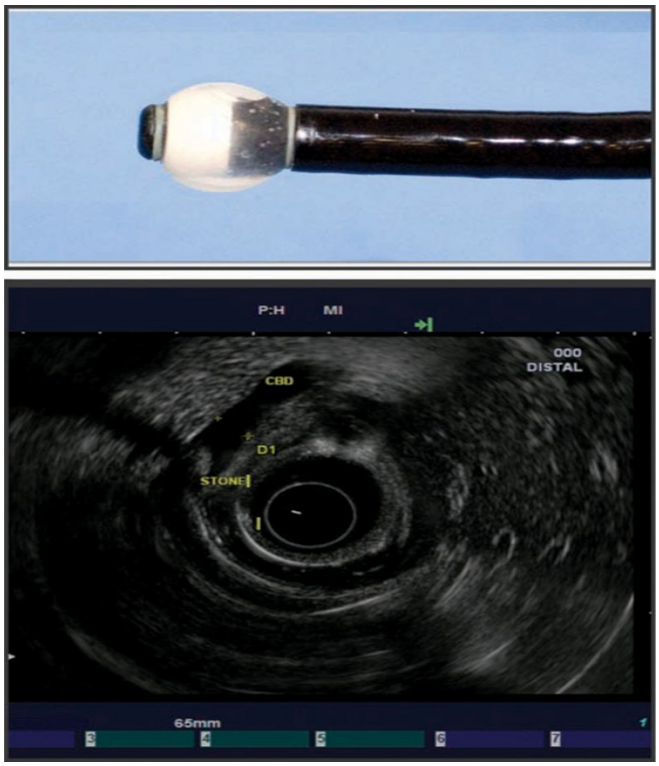

Figure 6: Radial EUS scope with EUS of bile duct stone (5).

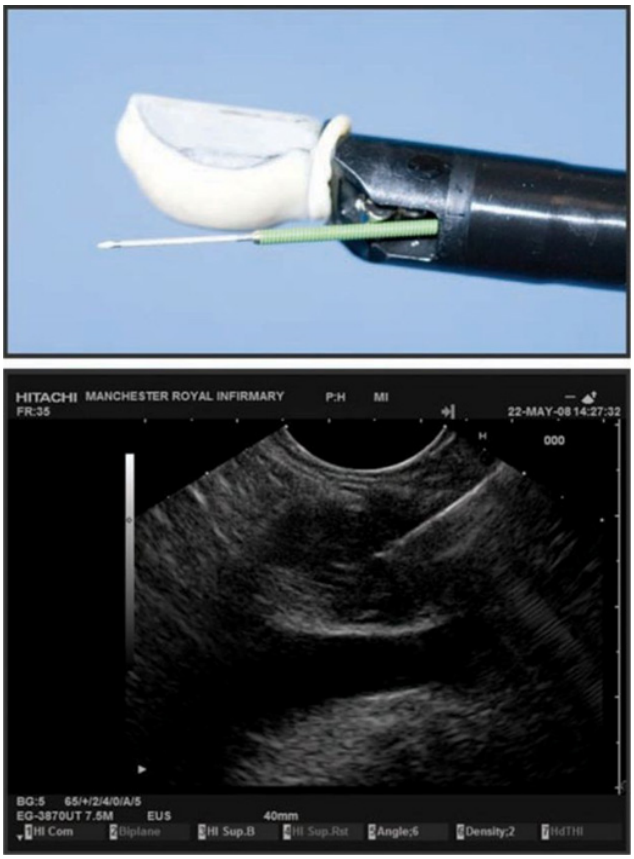

Figure 7: Linear EUS scope with FNA and pancreatic mass FNA (5)

essential element in the widely accepted TNM classification of GI malignancies due to its capability of separating the various layers of the GI tract wall **(5)**.

Pancreatic cancer

The high-resolution images produced by EUS allow for the detection of small tumors, cysts, and vascular invasion in the pancreatic duct and parenchyma with great sensitivity. EUS has a staging sensitivity of over 90%, surpassing spiral CT, MRI, and positron emission tomography (PET) in detecting small pancreatic tumors. This method is highly sensitive in identifying pancreatic neuroendocrine tumors, even able to distinguish entities as small as 2-3 mm **(23).**

Pancreaticobiliary Disease

Cystic lesions of the pancreas

As the availability of CT imaging has increased, the incidence of incidental cystic lesions of the pancreas has risen steadily. 10% of these lesions may contain malignant or premalignant neoplasms, whereas the majority are benign and of a benign nature. There has been no improvement in the capacity to distinguish benign cysts from malignant ones, even with the advent of CT and MRI. EUS offers the dual benefit of sampling the cyst material and any nearby lymph nodes in addition to providing high-resolution pictures. In cases of cystic lesions, the diagnostic accuracy can be enhanced by combining EUS-FNA with cytology **(24)**.

Chronic pancreatitis

While TAUS, CT, MRI, and ERCP may not reveal structural alterations associated with chronic pancreatitis, EUS is a very sensitive imaging modality that can. It is important to use caution when diagnosing age-related pancreatic alterations as early signs of chronic pancreatitis, though. Differentiating hypoechoic pancreatic mass from chronic focal pancreatitis in individuals suffering from chronic pancreatitis is frequently the biggest challenge in diagnostic interpretation. When this happens, a positive EUS-FNA is great, but surgery is usually necessary even when the test comes back negative for cancer due to its limited sensitivity **(25)**.

Mediastinal lymphadenopathy

Endoscopic ultrasonography allows for clear visualization of the aortopulmonary, subcarinal, paratracheal, and para-oesophageal lymph nodes. EUS-FNA of mediastinal nodes improves diagnostic accuracy in detecting malignant characteristics, thus avoiding the need for mediastinoscopy or thoracotomy. EUS-FNA can be employed to confirm the diagnosis when other diagnostic procedures like CT, PET, bronchoscopy, and pleurocenteses have been unsuccessful in yielding a positive result. This procedure has the ability to distinguish between TB, sarcoidosis, and lymphoma following EUS-FNA and trucut biopsy. Moreover, it has a high sensitivity of 88% to 96% in detecting malignancy in mediastinal lymph nodes. This obviates the necessity of performing invasive mediastinoscopy (26).

Therapeutic EUS

Exciting advancements in therapeutic applications of EUS have emerged from the initial research and progress made in EUS-

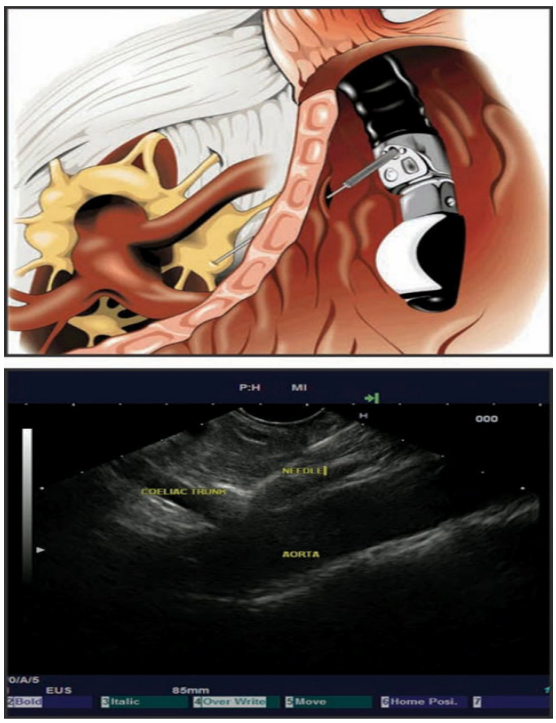

Figure 8: EUS coeliac ganglia neurolysis **(28)**.

FNA. The technique of EUS-guided injection, specifically targeting the coeliac plexus or celiac ganglia with steroids or alcohol, has proven to be a dependable and safe approach for pain control in cases of pancreatic cancer and, to a lesser extent, chronic pancreatitis (27).

Previously, the drainage of symptomatic pseudocysts was performed either blindly using a direct endoscopic method or with surgical intervention. EUS cystogastrostomy enables the identification of the pseudocyst, direct puncturing into the cyst with the guidance of EUS imaging (thus avoiding any blood arteries), and the insertion of a stent in a single procedure, all while reducing the length of the patient's hospital stay compared to surgery. If this option is available, it should be used to treat symptomatic uncomplicated pseudocysts. Following the failure of ERCP, the biliary system can be accessed via EUS. Under EUS supervision, a wire is punctured into the common bile duct to accomplish this. Even if a CT scan misses the ascites, an EUS can still locate it and drain it **(29)**. Various experimental uses of EUS are being examined. These include treating advanced pancreatic cancer with brachytherapy or chemotherapy, alcohol ablation for adrenal metastases or neuroendocrine tumors, and EUS-guided radiopaque marker implantation under the mucosal layer before radiotherapy. Normal orifice transluminal endoscopic surgery is rapidly merging endoscopy and surgery, with endoscopic ultrasonography (EUS) playing a key role **(30)**.

Somatostatin in treatment of of acute recurrent pancreatitis

There are two distinct forms of somatostatin (SS) found in people: one with fourteen amino acids and another with twenty-eight amino acids. It is a cyclic polypeptide. This hormone is generated by various cells in response to a range of stimuli, including neuropeptides, neurotransmitters, ions, nutrients, hormones, cytokines, and growth factors **(31).**

Cells that produce somatostatin-14 can be found in various peripheral organs such as the liver, pancreas, lungs, immune system, urogenital tracts, kidneys, and adrenals. On the other hand, SS-28 is primarily produced by mucosal epithelial cells lining the gastrointestinal tract. This hormone has a significant impact on various bodily functions. It has the ability to suppress pain, inhibit the release of hypothalamic hormones, decrease gastrointestinal activity, and reduce the release of T3/T4 in the thyroid. Multiple studies have demonstrated a clear connection between somatostatin and the secretory function of the pancreas. Expression of insulin, glucagon, and PP genes is reduced by somatostatin. This leads to a decrease in the production of hormones by the pancreas and hinders the release of bicarbonate and digestive enzymes from the pancreas **(31).**

The physiological effects of SS are achieved through the presence of transmembrane receptors known as the SSTR receptor family, which are connected to the G-protein. Mammals possess five subtypes of SSTR, namely 1–5 **(32).**

The physiological effects of somatostatin on the gastrointestinal tract, pancreas, and immune system are primarily mediated by receptors 2 and 5. Multiple studies have shown the expression of SSTR2 on α cells and SSTR5 on β cells. It indicates that SSTR2 plays a role in controlling glucagon secretion, while SSTR5 is involved in regulating insulin secretion. The secretion of insulin from the pancreatic β cells is strongly inhibited by Somatostatin-28. The SS-28 released from the stomach reduces insulin secretion after a meal, which helps prevent hypoglycemia and maintain insulin sensitivity in target tissues. In addition, SS-14, which is produced by δ cells, can also suppress the function of β-cells. Research has shown that SS-14 functions as a suppressor of gastrin and glucagon secretion **(33).**

Octreotide may change exocrine pancreatic secretion since it is a synthetic version of somatostatin. The exact way that somatostatin and octreotide affect this process remains unclear and requires more study. Somatostatin inhibits the release and manufacture of certain enzymes, which in turn decreases the pancreas' ability to absorb amino acids. The release of somatostatin from the pancreatic islets is stimulated by high glucose concentration. Somatostatin may have a function in pancreatic illnesses like diabetes. **(34).** The hormone somatostatin suppresses the exocrine function of the pancreas in both humans and animals. The effect is accomplished by reducing the release of hormones from glands and, by extension, by reducing the release of hormones from the gastrointestinal tract. Acute pancreatitis is characterized by the destruction of the pancreatic gland and the subsequent release of digestive enzymes into the circulation, which occurs when the pancreas is activated. This leads to signs of organ failure throughout the body. Theoretically, somatostatin's capacity to inhibit pancreatic enzyme release suggests it may be useful in acute pancreatitis. The production of pancreatic enzymes may be reduced by 76-70% when somatostatin is administered at a dose of 1*35 tg/kg/h.I understand. According to an other investigation, the pancreatic secretion was decreased by 40% when an infusion rate of 3 μg/h was used, with the maximum inhibition level reaching at a rate of 90 μg/h.Four Most patients received a dose of somatostatin comparable to 1-75 pig/kg/h or higher, suggesting that the amount used in this investigation was adequate **(35).** The therapy period may be insufficient for certain people. In a few cases, serum amylase levels increased after somatostatin was stopped. **(36).**

In instances of acute pancreatitis, the amount of inflammation and necrosis in the pancreas and peripancreas may be evaluated by measuring the blood LDH concentration, which is a marker of tissue damage. The somatostatin group had a much lower LDH level than the control group two days following hospitalization. Changes in serum LDH levels seen in the first two days. A total of nine patients in the somatostatin group had elevated LDH levels at admission, compared to six in the control group. Elevated LDH levels were seen in eight individuals in the control group two days after admission.

Three of these individuals had very high values to begin with, and five of them had a rise in their LDH levels over time. **(37).**

Elevated LDH levels were seen in five individuals in the somatostatin group two days after admission. Out of them, four had preexisting high concentrations and one had elevated LDH levels. Our results suggest that somatostatin therapy, especially when started before local inflammation and necrosis have started, successfully slows these processes. Because the local immune response was suppressed, the white blood cell count in the somatostatin group decreased after therapy**(38).**

Somatostatin may have beneficial effects on a local level, according to the available research. Some may ask how this may be used to treat pancreatitis. Somatostatin treatment is reserved for those who have local problems. For the best outcomes, it is advised to provide the medication prior to these issues occurring. In regions where pancreatic pseudocysts, abscesses, or necrosis are common, somatostatin therapy should be started immediately for all patients **(39).** Only individuals at high risk of experiencing severe problems should be given somatostatin. In order to determine what variables may be associated with the occurrence of complications in patients with acute pancreatitis, we are now analyzing their clinical data. Patients identified as having an increased risk of problems will undergo further somatostatin testing. Conservative therapy is usually sufficient for the management of acute interstitial pancreatitis, which usually resolves without further medical intervention. Consequently, it is associated with little risk of complications and death. Necrosis inside and around the pancreas occurs in a limited number of people who have acute pancreatitis.Having three Severe metabolic and systemic consequences, including organ failure and death, may occur as a consequence of toxic chemical release **(40).**

The activation of pancreatic digestive enzymes causes autodigestion, a hallmark of acute pancreatitis. Therefore, inhibiting the secretion of exocrine pancreatic enzymes to lessen pancreatic tissue self-digestion might be a therapeutic strategy for acute pancreatitis management. It is vital to ascertain if pancreatic secretion persists throughout the progression of acute pancreatitis before contemplating the use of drugs that block secretion as a therapy**(41).**

Acute pancreatitis may be categorized clinically as either moderate or severe. Acute pancreatitis is often mild and self-limiting, responding well to conservative therapy. The majority of people will suffer this condition. About 20% of individuals with acute pancreatitis progress to a severe type that includes extrapancreatic necrosis in addition to pancreatic necrosis. Despite the different treatment techniques presently available, patients with severe acute pancreatitis generally face systemic sequelae and a fatality rate ranging from 10% to 50%. In contrast, the morbidity and mortality rates for moderate acute pancreatitis are quite modest. The pathophysiology of acute pancreatitis is still being studied, even though little is known about it **(42).**

The common belief that the activation of digestive enzymes initiates acute inflammation was first described by Chiari in 1896 when he used the word "autodigestion" to characterize this idea. One possible treatment option for acute pancreatitis in humans is the hormone somatostatin, which blocks exocrine pancreatic output. This hypothesis was tested in a randomized controlled experiment. Significant clinical improvement was shown by the trial's outcomes. Researchers are still debating the efficacy of somatostatin after subsequent randomized studies in cases of acute pancreatitis. Somatostatin therapy reduced death rates significantly, from 14% to 6.2%, according to a meta-analysis of well-designed trials. Acute pancreatitis' inflammatory phase has no effect on basal exocrine secretion, according to previous research.2021 Octreotide is a synthetic somatostatin analogue that has the ability to cure acute pancreatitis, and this study's results have sparked a lot of interest in its possible therapeutic use. Three different dosages of octreotide (100, 200, or 500 μg three times day) were administered to individuals with mild to severe acute pancreatitis in a research. Particularly in the group that received 200 μg, the data demonstrated a discernible reduction in the incidence of new problem **(43).**

CONCLUSION

Therapeutic EUS procedures, assessment of pancreaticobiliary illness, evaluation of subepithelial abnormalities, evaluation of extraluminal abnormalities, or staging of gastrointestinal cancers are among the many indications for EUS. In comparison to other imaging techniques such as spiral CT, MRI, and PET, EUS is superior in terms of its sensitivity when it comes to detecting tiny tumors, cysts, and vascular invasion. Researchers are still debating the efficacy of somatostatin after subsequent randomized studies in cases of acute pancreatitis. Somatostatin therapy reduced death rates significantly, from 14% to 6.2%, according to a meta-analysis of well-designed trials.

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