EASTERN PENNSYLVANIA GASTROENTEROLOGY AND LIVER SPECIALISTS

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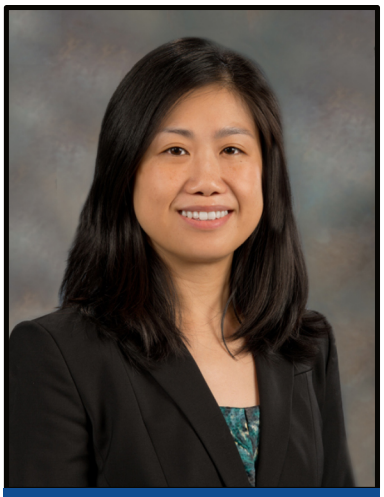


SHE-YAN WONG, MD

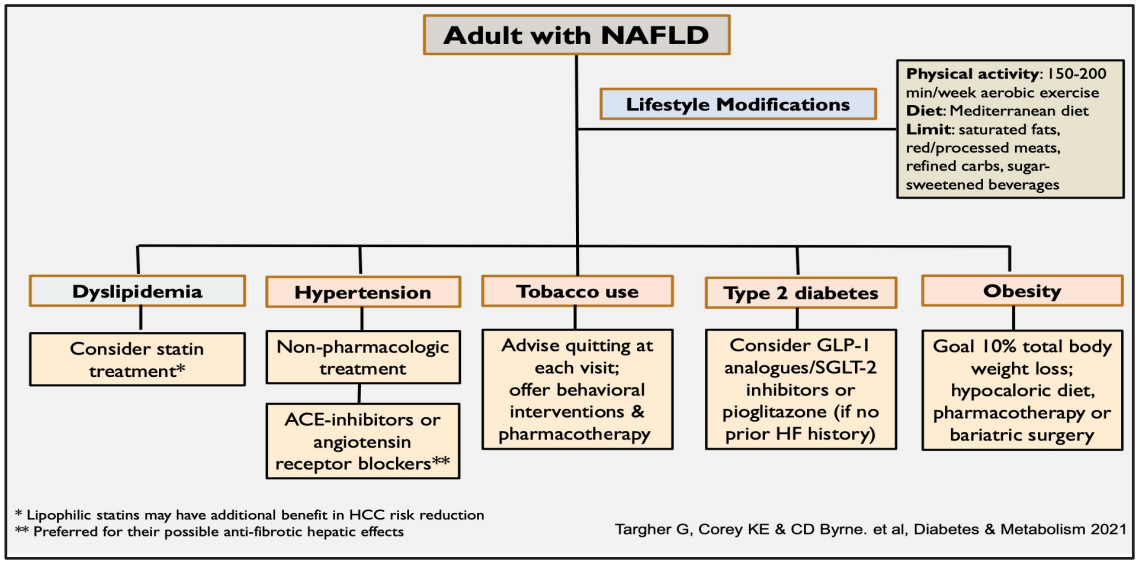
IN THIS EDITION

UPDATES FROM THE LIVER MEETING (AASLD 2021)

This year, the AASLD liver meeting took place virtually and highlighted the epidemic of fatty liver disease due to obesity and alcohol. Though FDA approved medications are not yet available for NAFLD (non-alcoholic fatty liver disease), the course focused on mitigating risk factors associated with the disease as well the growing impact of alcohol on the liver. Management of fatty liver disease often is multidisciplinary, starting from the primary care practitioner to the gastroenterologist/hepatologist, and may include endocrinology, cardiology, and bariatric surgery. With a growing prevalence of NAFLD, which is at 25% currently in the United States, it is a disease that most practitioners will encounter.

NAFLD and diet

The mainstay of treatment is still lifestyle modification focusing on diet and weight loss (See Table below). It is known from previous studies that a 10% weight reduction can reverse steatosis, inflammation and even fibrosis (1). Individualizing diets and maintenance of weight loss is key to treatment. The Mediterranean diet has been shown to be effective in decreasing hepatic fat (2).



Intermittent fasting and keto diets have been utilized for rapid weight loss. However, limited data is available to suggest its long term use in NAFLD. Overall recommendations include:

1. Limiting ultra-processed foods
2. Limiting saturated fats
3. Limiting sugar (fructose and sucrose)
4. Increasing phenolic acid rich foods (coffee, fruits, vegetables, seeds, nuts)

Management of NAFLD

Other updates include potential nomenclature change of NAFLD to MAFLD (metabolic associated fatty liver disease) to more accurately represent the disease pathogenesis and potential treatments. Genetics also will likely play more of role in treatment targets. Mutations in the PNPLA3 gene have been associated with NAFLD.

Alcohol related liver disease and liver transplantation

Alcohol related liver disease continues to be a significant problem, accounting globally for 50% of all deaths from liver disease. It is therefore important to identify patients early with alcohol use disorder and related liver disease and counsel them. Efforts are ongoing to improve this, which includes destigmatizing the disease and increasing detection with biomarker testing. While blood and urine ethanol levels remain for less than 24 hours, phosphatidylethanol (PEth) levels can detect alcohol use as well as quantify the degree of consumption for up to 3-4 weeks. PEth testing is currently available and increasingly being used in clinical practice. Medical treatment for alcohol related liver disease is limited. Steroids are indicated for severe disease (Maddrey's Discriminant Function > 32 or MELD > 21). However, only about 50% will respond to steroid therapy as calculated by a day 7 Lille score. Non-responders have a 75% mortality, which has led to liver transplantation as a potential option for select patients.

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SHASHIN SHAH, MD

ENDOSCOPIC DIAGNOSIS AND MANAGEMENT OF AMPULLARY AND PANCREAS CANCER

An estimated 60,000 new diagnoses of pancreas cancer were made in 2021 in the United States, accounting for three percent of all cancers (1). Most of these diagnoses were made by gastroenterologists specializing in endoscopic ultrasound (EUS). When a patient with a pancreas mass is evaluated by an advanced endoscopist, it involves establishing the diagnosis and then determining the best approach to optimizing disease management and the quality of life for the patient.

After taking a comprehensive history inclusive of risk factors and family history and then reviewing prior imaging, we embark on a path with the patient, family and the patient's providers. EUS offers the ability to "see" the pancreas through a thin wall of either the stomach or duodenum. EUS can determine the proximity of a pancreas mass to surrounding vasculature such as the celiac artery, superior mesenteric artery or portal vein and offers insight into the potential for immediate respectability.

The liver, surrounding lymph nodes and even ascites can also be sampled via EUS and Fine needle Aspiration (FNA) to mitigate the potential for spread of the primary tumor.

Sensitivity for diagnosing pancreatic malignancy by this approach was 92% and specificity was 96% in a meta-analysis (2). These findings are interpreted in conjunction with cross sectional imaging such as CT scan and MRI to help stage the patient for subsequent therapeutic decisions. **ERCP with brushings** can also assist in the diagnosis of pancreas head tumors if there is infiltration of the bile duct. Once a diagnosis of pancreas cancer is made, the patient may need additional advanced endoscopic management.

Ampullary masses arise in the ampulla of vater which is just distal to where bile duct and pancreas duct join and drain into the duodenum. If detected at an early precancerous or adenomatous stage, these lesions can often be evaluated with EUS and removed with **endoscopic ampullectomy** (snare resection). This method can cure the lesion and prevent cancer of the ampulla. In cases where a cancer of the ampulla already exists, treatment often requires surgery and is managed similarly to how pancreas cancer is managed. (1)

In cases of unresectable or borderline resectable tumors, certain forms of oncologic radiation treatments may be enhanced with **EUS guided injection of gold fiducials** (markers) placed to help localize the tumor for CT guided radiation, minimizing radiation injury to normal surrounding tissues.

If the patient has severe abdominal pain due to a non-operable pancreas body/tail tumor burden, we can offer an **EUS guided pain block or celiac plexus neurolysis (CPN)**. Using a specialized needle, we inject an anesthetic such as bupivacaine and 98% alcohol into the nerve bundle that is infiltrated by the tumor to lessen the pain, restore quality of life and minimize narcotic use. The pain block typically can help 50-80 percent of patients for up to 2-3 months (3,4). This procedure can be repeated for recurrence of pain if initially successful.

Additionally, placement of a self-expandable metal stent (SEMS) can alleviate pruritus and jaundice in patients with pancreas head tumors or lymph nodes that are compressing the biliary tree.

In select cases, if access to the bile duct via the major papilla for ERCP is compromised due to anatomy or tumor, direct bile duct access with an EUS guided duodenal puncture technique can be used for bile duct access and management. This technique is higher risk and can lead to bile peritonitis and duodenal perforation. Optimizing technology for this technique is currently being studied.

EUS and ERCP serve key roles in the diagnosis, management and treatment of ampullary lesions and pancreas cancer. Furthermore, tumors of the head or uncinate portion of the pancreas can erode into and involve the lumen of the duodenum causing a gastric outlet obstruction type process. If the patient is non-operable at this point, an **endoscopically placed duodenal stent** can allow the patient to eat and to avoid a surgical feeding tube or palliative gastro-jejunal bypass.

Many of the above procedures or a combination thereof can be done in a single endoscopic setting or two. Repeat procedures may be necessary as the tumor progresses or the patient's clinical status changes.

Endoscopic management of pancreas cancer and ampullary lesions can help diagnose, stage, relieve jaundice and serve a pain management and palliative role to allow the patient to have dignity, comfort and proceed to the next steps in management with their oncologic providers.

MATTHEW SULIVAN, DO

ESOPHAGEAL DIAGNOSTIC TESTING IN THE MANAGEMENT OF GERD

The classic symptoms of gastroesophageal reflux disease (GERD) are pyrosis ("heartburn") and/or regurgitation. However, patients may also report atypical or overlap symptoms of chest pain, epigastric pain, dyspepsia, nausea, bloating or belching, as well as extra-esophageal symptoms including chronic cough, worsening asthma or chronic laryngitis. GERD is diagnosed through a combination of symptom presentation, endoscopic evaluation of the esophageal mucosa, reflux monitoring and response to therapeutic intervention. This article will focus specifically on reflux monitoring and high-resolution esophageal manometry (HREM) and the role they play in establishing a diagnosis of GERD.

Establishing a Diagnosis of GERD

According to the recently updated guidelines from the American College of Gastroenterology, reflux monitoring should be used to confirm a diagnosis of GERD in patients with symptoms suggestive of GERD, but in the absence of significant esophagitis (Los Angeles grade B, C, or D) or Barrett's esophagus, both of which confirm the presence of GERD. There are two main options for reflux monitoring, wireless pH monitoring and transnasal catheter-based pH/impedance monitoring. Both studies allow for the assessment of esophageal acid exposure time (EAET), the number of individual reflux events and symptom correlation with reflux events. But there are important differences regarding the information obtained and patient comfort/acceptance. The wireless pH monitor is placed during esophagogastroduodenoscopy (EGD), usually under anesthesia, and continually records the pH in the location in the esophagus where it is placed (typically 6 cm above the gastroesophageal junction) for 48 hours. It can be performed up to 96 hours with more specialized equipment. Catheter-based pH/impedance monitoring is performed by placing the catheter transnasally and it remains in place for 24 hours. During either study, patients are encouraged to practice their normal daily routine. Catheter-based testing has the added advantage of impedance monitoring, which allows for the detection of non-acid or weakly acidic reflux, as well as calculation of the mean nocturnal baseline impedance, a value that can predict response to anti-reflux therapy. However, catheter-based testing is often not readily accepted by patients due to discomfort, an overactive gag reflex and/or the embarrassment of the transnasal catheter. Either study is appropriate as the initial study to document the presence or absence of GERD. When establishing a diagnosis of GERD, reflux monitoring should be performed off proton pump inhibitor (PPI). It is recommended that PPI be held for 7 days prior to the study (histamine 2 receptor antagonists should be held for 5 days). If the study reveals pathologic EAET with significant symptom correlation, the diagnosis of GERD is established. Reflux monitoring can also be utilized to rule out GERD when clinical suspicion is low. Patients may be categorized as having reflux hypersensitivity (physiologic EAET, but with symptom correlation) or functional heartburn (physiologic EAET without symptom correlation). In these situations, pathologic GERD is ruled out. Occasionally the study may show pathologic EAET, but no symptom correlation. This scenario confirms the presence of GERD but may require additional investigation as treatment of the reflux may not lead to improvement of the reported symptoms.

Investigating Potentially Reflux-Related Symptoms

Reflux monitoring can also be helpful in patients with an established diagnosis of GERD. Patients reporting symptoms that are potentially reflux-related but are not responding to PPI or a prior anti-reflux procedure can benefit from reflux monitoring. In this scenario, the recommended study is catheter-based pH/impedance monitoring, and this can be performed while the patient is still taking PPI. This allows for the detection of symptom correlation with breakthrough acid reflux or either non-acidic or weakly acidic reflux. Extra-esophageal symptoms such as chronic cough and globus sensation are also commonly reported and reflux monitoring can be a beneficial diagnostic tool here as well. If the patient does not have known GERD, testing can be performed either on or off PPI, but catheter-based pH/impedance is the preferred study. Wireless pH testing only focuses on distal acid reflux and is not a reliable study to detect potential laryngeal acid exposure. In addition to being able to detect both acid and non-acid reflux, catheter-based pH/impedance testing can determine the extent of proximal reflux. Dual sensor catheters with an oropharyngeal pH sensor do exist, but its reliability is questioned in the literature and it is therefore not commonly utilized.

Role of Esophageal Manometry

HREM assesses the lower esophageal sphincter pressure and relaxation, esophageal body contraction vigor and pattern, and bolus clearance from the esophagus. HREM is not a diagnostic test for GERD and there are no specific manometric abnormalities that are specific for GERD. However, manometry is a complementary study in the management of GERD, most commonly when anti-reflux procedures are considered. Esophageal manometry can identify achalasia which can present with similar symptoms but has a drastically different therapeutic approach. It can also identify other disorders of esophageal motor function, such as ineffective esophageal motility or jackhammer esophagus that may increase the risk for post-operative dysphagia. This information can influence which anti-reflux procedure is ultimately performed or even identify patients for whom anti-reflux surgery is not appropriate. Esophageal manometry may also be useful in patients with refractory GERD despite medical therapy. Conditions such as achalasia, esophageal spasm, and absent contractility can present with heartburn symptoms and these conditions can be ruled out with manometry.

In summary, reflux monitoring and HREM can provide clarity in establishing a diagnosis of GERD and guide management. Choosing the optimal study is dependent on the clinical question being asked and an individualized approach is recommended.

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1501 N. Cedar Crest Blvd
Suite 110
Allentown PA, 18104

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Before 2011, only five centers were performing liver transplantation for alcohol related hepatitis. In 2021, this has increased to 73 (50%) centers in the United States (3). Though the rate has increased significantly, it only accounts for 2% of all transplants performed. Criteria for selection are very stringent. Eligibility is based on multiple factors, including psychosocial issues, prior decompensating events and family support, which are evaluated by a multidisciplinary transplant team. The SIPAT (Stanford Integrated Psychosocial Assessment for Transplant) score can be a helpful tool in determining risk (4). Outcomes of liver transplantation have been good, even with improved survival compared to other indications for liver transplant. Return to harmful drinking has been shown to be uncommon, about 12%, and loss of graft or mortality due to this is even lower at 0-3%. Transplantation for alcohol related hepatitis will continue to be debated and criteria for appropriate candidates will evolve over time.

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