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# EUS-guided tissue acquisition of liver and hepatobiliary masses

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ABSTRACT

Endoscopic ultrasound (EUS) is increasingly used in the evaluation of hepatobiliary lesions and for obtaining liver biopsies. EUS-guided tissue acquisition is safe and effective, with high diagnostic yield and low major complication rate. This article reviews the techniques and clinical outcomes of EUS-guided tissue acquisition of hepatobiliary masses as well as EUS-guided liver biopsy.



## 1. Introduction

Endoscopic ultrasound (EUS) has become the first line modality in the evaluation of pancreaticobiliary lesions, and is increasingly considered in the evaluation of intrahepatic lesions and as a modality for obtaining liver biopsies. Here we discuss the techniques and clinical outcomes of EUS-guided tissue acquisition of hepatobiliary masses as well as EUS-guided liver biopsy. The literature reviewed in this article includes frequently cited studies relevant to the topic chosen at the discretion of the authors.

## 2. Hepatobiliary masses

EUS allows for the targeted biopsies of focal lesions throughout the liver and biliary system, and may have a valuable role in the tissue acquisition of various hepatobiliary lesions, especially those that are poorly accessible to other imaging modalities [1,2].

### 2.1. Liver metastases

The current diagnostic test of choice for the detection of metastatic lesions in the liver includes computed tomography (CT) and magnetic resonance imaging (MRI). These radiographic modalities are limited in their ability to detect small lesions $< 1$ cm in size [2]. Although EUS does not have the ability to completely visualize the entire liver and is thus not feasible as a screening mechanism for metastatic disease, EUS does have the ability to detect small hepatic lesions that may otherwise be missed by CT or MRI, and can detect tumors less than 3 mm in size [3]. EUS can provide detailed examinations of the liver from the transgastric and transduodenal routes, and is able to visualize the majority of the liver with the exception of the right posterior segments [4].

The major advantage of EUS is the ability to perform fine-needle aspiration (FNA) for tissue acquisition of suspicious liver masses. Initial experience on EUS-FNA of liver masses was described by Nguyen et al. [5]. In an evaluation of 574 patients with suspicion of pulmonary or gastrointestinal malignancy, 14 (2.4%) were found to have a focal liver lesion and underwent EUS-FNA with a 22-gauge needle (GIP, Mediglobe, Tempe, AZ). A total of 15 samples were obtained, of which 14 were malignant and a new diagnosis of cancer was made in 7 patients. In comparison, pre-endoscopic CT was able to identify liver lesions in only 3 of these 14 patients. There were no major complications. The findings of this study showed the value of EUS-FNA in identifying and confirming suspected liver metastatic disease diagnosis and potentially changing clinical management.

EUS-FNA may also be useful when conventional CT or trans-abdominal ultrasound-guided FNA are unsuccessful or non-diagnostic. A survey-based study by ten Berge et al. [6] showed that EUS-FNA was able to diagnose malignancy in 23 of 26 cases (89%) following non-diagnostic percutaneous ultrasound-guided FNA. There was a 4% complication rate, which included fever, pain, bleeding, and one case of death from biliary sepsis from an occluded biliary stent.

DeWitt et al. [7] reported a large single center study of EUS-FNA of 77 liver lesions. Of these lesions, 45 were found to be diagnostic for malignancy (the majority from pancreatic adenocarcinoma), 25 were benign, and 7 were non-diagnostic. No major complications were reported. Depending on the status of the non-diagnostic lesions, the reported sensitivity for EUS-FNA for the diagnosis

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of liver malignancy ranged from 82%-94%. Notably, EUS-FNA diagnosed malignancy in 41% of patients who previously had negative CT and/or abdominal ultrasound. EUS-FNA was found to change management in 86% of patients who were found to have malignancy, raising the conclusion that EUS-FNA may have the potential to substantially impact patient management. A separate study from Hollerbach et al. [8] demonstrated a high diagnostic yield for EUS-FNA of liver lesions. In their study of 41 patients with liver masses, EUS-FNA provided appropriate biopsy specimens in 40 cases, with an average of 1.4 needle passes. There were 2 minor complications of self-limited local bleeding.

Although EUS is primarily utilized to evaluate lesions in the left lobe of the liver, it can also safely and effectively evaluate lesions in the right liver lobe. This was demonstrated in a study from Oh et al. [9], in which EUS-FNA was performed on 47 patients with liver masses, including 17 in the right liver lobe. The overall technical success rate was 97.9% and diagnostic yield was 90.5%. When comparing outcomes between lesions in the left and right lobes, technical success, tumor size, and median needle passes were not significantly different. Adequate specimen was statistically higher in the left lobe than the right lobe (93.3% vs 82.4%, $P = 0.04$), however diagnostic accuracy was not different between the left and right lobes (89.3% vs 92.9%, $P = 0.86$), suggesting that EUS-FNA was feasible even for lesions in the right lobe.

Several studies have compared EUS and CT for the detection of liver metastases. In one such study, Singh et al. [10] prospectively evaluated 132 patients with newly diagnosed tumors of the lung, pancreas, biliary tree, esophagus, stomach, and colon. Liver metastases were established in 26 patients, of which the diagnostic accuracy of EUS and CT were 98% and 92%, respectively ($P = 0.0578$). Compared to CT, EUS detected a higher number of metastatic lesions in the liver (40 vs 19, $P = 0.008$). In 8 cases, CT detected lesions in the liver that were too small to characterize; of those, EUS-FNA correctly identified the lesions as malignant in 3/3 cases and benign in 4/5 cases, with no reported complications. The results of this study as well as the other studies reviewed in this article suggest a potential role for EUS-FNA in the evaluation of liver metastases, particularly those too small to be characterized by conventional radiographic means.

### 2.2. Hepatocellular carcinoma

Although hepatocellular carcinoma (HCC) can be typically diagnosed based on characteristic CT and MRI findings alone, current radiologic modalities are limited by their ability to detect small lesions. Several small single center studies have therefore examined the feasibility of EUS-FNA for the diagnosis of HCC. Awad and colleagues reported a series of 14 patients who underwent EUS for evaluation of suspected liver malignancy including HCC. In all 14 patients, EUS was able to successfully identify hepatic lesions ranging from 0.3 to 14 cm in size, and EUS was able to identify new or additional lesions in 28% of these patients. Nine of the 14 patients underwent EUS-FNA with 2 needle passes, in which all FNA passes yielded adequate specimen and 8 were diagnosed as malignant, including 3 cases of HCC.

In a separate study, Singh et al. [11] compared the accuracy of EUS with CT for the detection of HCC. A total of 17 patients were deemed to be high risk for HCC based on laboratory and radiographic findings and were enrolled into their study. In all, 9 of the 17 patients were found to have liver tumors (8 with HCC and 1 with cholangiocarcinoma). EUS-FNA was able to establish a tissue diagnosis in 8 of the 9 cases, with no report of major complications. EUS-FNA overall had a diagnostic accuracy of 94% and EUS detected a significantly higher number of lesions than ultrasound, CT, or MRI. The findings of these studies suggest a role for EUS in the diagnosis of patients with suspected HCC.

### 2.3. Biliary strictures

Although magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography are the primary modalities for the evaluation of biliary strictures, EUS may have an important role particularly when first line studies are inconclusive [12]. Several series have reported on the performance characteristics of EUS-FNA for diagnosing extrahepatic cholangiocarcinoma. DeWitt et al. [13] and colleagues evaluated the role of EUS-FNA of proximal biliary strictures after negative endoscopic retrograde cholangiopancreatography brush cytology. Of 24 patients who underwent EUS-FNA, of which a mass was visualized in 23 (96%) patients, including 13 in whom previously imaging had not detected a lesion. EUS-FNA demonstrated malignancy in 17 (71%) patients, with findings showing adenocarcinoma in 15 and lymphoma in 2 patients. The overall sensitivity and specificity for EUS-FNA was found to be 77% and 100%.

A systematic review and meta-analysis including 20 studies involving 957 patients found the pooled sensitivity and specificity for EUS-FNA for diagnosis of malignant biliary strictures were80% and 97% [14]. However, it is to be noted that some centers disqualify patients for liver transplantation if EUS-FNA has been performed, given concern for tumor seeding with the technique [15]. Therefore, EUS-FNA is contraindicated in patients with suspected hilar or perihilar cholangiocarcinoma who may be transplant candidates.

### 2.4. Gallbladder lesions

EUS is generally considered superior to other imaging modalities in detecting malignant gallbladder polyps, and has an expanding role in the diagnosis and staging of gallbladder adenocarcinoma. However, data on EUS-FNA of the gallbladder wall is very limited. One reported study from Meara et al. [16] prospectively evaluated the performance characteristics of EUS-FNA of 7 patients with gallbladder lesions using a 22-gauge needle. All 7 patients were found on EUS-FNA to have carcinoma, with a reported sensitivity of 80% and specificity of 100%.

Varadarajulu and Eloubeidi [17] reported a retrospective series of 6 patients who underwent EUS-FNA of gallbladder masses, in which only 1 had been found on CT to have a gallbladder mass and none had been found to have a gallbladder mass on abdominal ultrasound. On EUS, all 6 patients were found to have a mass arising from the gallbladder wall or within the lumen of the gallbladder, and on EUS-FNA, 5 were found to have adenocarcinoma and 1 was found to have benign disease (found at surgery to have chronic cholecystitis), with no major complications. Similarly, Jacobson et al. [18] also reported a retrospective series of 6 patients who underwent EUS-FNA of gallbladder masses. On EUS-FNA, 3 patients were positive for adenocarcinoma, 1 had cytology suspicious for adenocarcinoma (confirmed surgically), 1 had atypical cells (confirmed surgically to have adenocarcinoma), and 1 was found to have benign disease (found at surgery to have xanthogranulomatous cholecystitis), with no major complications. At this time, larger studies evaluating the role of EUS-FNA in tissue acquisition of gallbladder lesions are needed.

## 3. Liver biopsy

The histological assessment of the liver has long been considered a cornerstone in the evaluation and management of patients with various liver diseases. According to the American Association for the Study of Liver Diseases (AASLD), the 3 major roles for liver biopsy include diagnosis of various liver diseases, assessment of prognosis including staging of fibrosis, and assistance in