"BENIGN AND MALIGNANT BILIARY STRICTURES: A COMPREHENSIVE REVIEW OF DIAGNOSIS AND TREATMENT."

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Annotation: Biliary strictures are characterized by a narrowing of the bile ducts that leads to obstruction and may arise from either benign or malignant conditions. Establishing an accurate diagnosis remains essential yet difficult, as benign and malignant strictures often present with overlapping clinical and radiological features. This review outlines a comprehensive diagnostic framework that combines biochemical markers, imaging techniques, and advanced endoscopic methods to differentiate between these etiologies. Commonly utilized imaging modalities, including ultrasound, MRI/MRCP, and contrast-enhanced computed tomography (CECT), each offer specific benefits and limitations. In addition, endoscopic approaches such as ERCP and EUS play a pivotal role in tissue sampling, thereby improving diagnostic precision, particularly in cases of indeterminate or complex strictures. Emerging technologies, including artificial intelligence and novel endoscopic innovations, demonstrate significant potential in enhancing diagnostic accuracy and minimizing uncertainties. Overall, this review highlights the importance of a multidisciplinary approach to optimize diagnostic pathways and facilitate timely and appropriate management of patients with biliary strictures.

Keywords: CECT; ERCP; EUS; MRI/MRCP; artificial intelligence; biliary strictures; cholangioscopy; tumor markers.

Introduction: A biliary stricture is defined as a narrowing of the bile ducts within the hepatobiliary system, which can impair bile flow and lead to significant clinical and physiological consequences. This obstruction frequently causes upstream dilatation of the biliary tree, resulting in both structural changes and symptoms associated with cholestasis. Although some cases are asymptomatic and detected incidentally on imaging, others present with clinical manifestations such as pruritus and jaundice .

Biliary strictures may arise from either benign or malignant etiologies, with malignancies—both primary and metastatic—representing a substantial proportion and carrying important diagnostic and therapeutic implications. In patients without a detectable mass on cross-sectional imaging, the likelihood of malignancy remains considerable. Benign strictures are typically characterized by smooth, symmetric, and tapered margins, whereas malignant strictures tend to exhibit irregular, asymmetric borders with shouldering and often involve longer ductal segments. Additionally, malignant lesions commonly demonstrate contrast enhancement on imaging .

Despite these distinguishing features, overlap between benign and malignant strictures is frequent, making definitive diagnosis challenging and often necessitating histological confirmation through tissue sampling. Therefore, evaluation of biliary strictures requires a comprehensive and integrative approach that combines biochemical markers, cross-sectional imaging modalities such as CT and MRI, and advanced endoscopic techniques for direct visualization and biopsy.

Diagnostic modalities

Cross-sectional imaging constitutes a fundamental initial step in the diagnosis of biliary strictures, playing a pivotal role in determining the stricture's location and the underlying cause of the obstruction, as noted by Dumonceau et al. Given the diagnostic complexities associated with this condition, research in the field has underscored the necessity of precise imaging to ascertain the severity and potential etiology of the stricture. According to the ACG guidelines, Magnetic Resonance Imaging (MRI) with Magnetic Resonance Cholangiopancreatography (MRCP) is recommended as the first-line imaging modality for evaluating biliary strictures, specifically to assess the level of the stricture and detect any associated masses that might provide insights into the benign or malignant nature of the stricture. The guidelines strongly emphasize the importance of identifying potential malignancies before advancing to subsequent steps, ensuring that these steps are focused and effective. The ASGE guidelines suggest the use of computed tomography (CT) and MRI as initial diagnostic tools, particularly in cases of suspected malignant obstruction. Nonetheless, this guideline places significant emphasis on the application of Endoscopic Retrograde Cholangiopancreatography (ERCP) for both diagnostic and therapeutic purposes, especially in cases necessitating drainage. This recommendation largely arises from ERCP's reputation as a versatile diagnostic and therapeutic modality, enabling simultaneous stricture diagnosis and therapeutic intervention, including stent placement or bile duct decompression, which can alleviate symptoms and prevent further complications .However, it is important to note that the modern paradigm discourages the use of ERCP solely for diagnostic purposes in biliary strictures because of its associated risks .Similar to the ACG guidelines, the ESGE guidelines recommend the use of a combined MRI/MRCP approach as the initial imaging modality. The ESGE guidelines also highlight the utility of ERCP for diagnostic and therapeutic interventions, particularly when combined with endoscopic ultrasound-guided tissue acquisition (EUS-TA). A key recommendation from the ESGE is to combine EUS-TA with ERCP-based sampling, ideally in a single session.

The role of tumor markers

Across all three guidelines, there is a consensus against the exclusive reliance on tumor markers for the diagnosis of biliary strictures due to their inadequate definitive diagnostic performance. The primary concern with carbohydrate antigen 19–9 (CA 19–9) and carcinoembryonic antigen (CEA) in diagnosing biliary strictures is their lack of specificity; elevated levels are not exclusive to pancreaticobiliary cancers and can be significantly elevated in various benign conditions that often mimic or coexist with malignant strictures. The ESGE guideline reinforces this position by presenting a meta-analysis that quantifies the issue, showing a pooled accuracy of 81% for CA 19–9 and 70% for CEA. Diagnostically, an accuracy range of 70–81% is considered insufficient to definitively rule in or out a life-altering diagnosis such as malignant biliary strictures. The findings of this meta-analysis indicate unacceptably high rates of both false positives, which can lead to unnecessary invasive procedures and patient anxiety, and false negatives, which provide a dangerous false sense of security. Consequently, regarding the use of CA and CEA as tumor markers for biliary strictures, the ESGE guidelines classify this recommendation as 'conditional' based on 'very low-quality evidence,' reflecting the inherent weaknesses and biases in the observational studies that constitute the body of literature on these tumor markers. In the context of the ACG and ASGE guidelines, the use of CA and CEA tumor markers is considered to be complementary. They are recommended in instances of clinical suspicion, where markedly elevated CA 19–9 levels (e.g. > 1000 U/mL) in the appropriate clinical context can heighten suspicion for malignancy and justify proceeding with invasive diagnostic tests such as EUS or ERCP. Additionally, in patients with an established diagnosis of malignant strictures, CA 19–9 measurements can be useful for monitoring treatment response or early recurrence following curative resection.

Conclusion

This analysis highlights a robust transatlantic consensus on the fundamental principles for managing biliary strictures: the superiority of MRI/MRCP, the ineffectiveness of tumor markers alone, the primacy of EUS for diagnosing distal masses, and a recommendation against routine preoperative drainage. The most notable and clinically significant divergence pertains to the management of perihilar strictures, where the ACG/ASGE's absolute contraindication of EUS-FNA due to seeding risk contrasts with the ESGE's more conditional and patient-specific approach. Additionally, the ESGE's emphasis on environmental sustainability represents a novel and necessary advancement in guidelines development. Clinicians should thus interpret these guidelines not as conflicting but as complementary frameworks that necessitate integration with local expertise, resource availability, and, most importantly, individual patient values and care objectives.

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