Editorial

Cystic liver lesions: from diagnosis to recognition of complications and when to treat

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In October 2022, the European Association for the Study of the Liver (EASL) published in Journal of Hepatology the Clinical Practice Guidelines (CPG) in regard to the diagnosis and management of cystic liver diseases (1). American College of Gastroenterology published similar guidelines in 2014 regarding focal liver lesions, but this is the first comprehensive guideline focusing on cystic liver lesions with robust background support and knowledge (2). An expert multidisciplinary panel developed the guidelines based on extensive literature review and their experience and expertise, and provided a ranking of quality of evidence for each recommendation (1). Recommendations were graded as strong if they fit criteria of good evidence and were graded as weak or open without much supporting evidence for use for cystic liver lesions (1).

This CPG specifically point out most appropriate imaging techniques and modalities in diagnosing cystic liver lesions with some potential for differentiation between simple and complex cysts (1). Ultrasound (US) has been described as gold standard for initial diagnosis of cystic liver lesion, however incidental findings on both US and computerized tomography (CT) scan also occur (3). Homogenous and hypoattenuating lesions are often described and the size of the lesion is important in regard to liver volume. Magnetic resonance imaging (MRI) can be useful to differentiate simple versus complex cystic lesions, and are more commonly used for diagnosis in biliary disease particularly magnetic resonance cholangiopancreatography (MRCP) (1).

The authors uniquely highlight the importance of the quantity and quality of lesions to classify hepatic cystic lesions (1). Location is also important. When cysts grow, compression can occur leading to complications including cholestasis, portal hypertension or Budd-Chiari syndrome (3). Follow up of lesions is only indicated if there are complications or symptoms (1). The guideline explicitly indicates treatment depending on the type, size, location, complexity, and complications of the lesions. This is of benefit to provide an overview of approach to these lesions, however in practical medicine there remains a lot more variability and confounding factors. Guidelines can do just that, provide guidance, but with vague overtone it can be difficult to decide what to do at times.

Cystic liver disease has a prevalence of 2–18% of the population with rates increasing as people age (4-6). Females are more commonly affected with a concern of some impact from estrogen leading to increase in number of cysts (6,7). The most common entity is simple hepatic cysts that are often seen incidentally and are mostly asymptomatic (4). Genetic diseases such as autosomal dominant polycystic kidney disease (ADPKD) and polycystic liver disease (PLD) can also present with

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a few to several cystic liver lesions (1). Overlap between ADPKD and PLD is very common, with greater than 90% of patients with ADPKD will have extrarenal lesions with most common being liver lesions (8,9). Therefore, EASL and nephrology societies agree upon careful selecting of imaging with abdominal US screening for PLD in all patients with confirmed ADPKD to avoid contrast agents (1). Genetic testing is less useful for diagnosis of PLD with only about 30–45% of patients having an identified gene on screening (1).

While several types of cystic liver lesions described have no connection to the biliary system, others do have biliary connection which can be localized or multi-segmental with dilation of intrahepatic ducts (10). With these, there is a higher concern for congenital hepatic fibrosis that often presents in childhood called Caroli syndrome and can be associated with Autosomal Recessive Polycystic Kidney Disease (ARPKD) (1). It is important to distinguish Caroli syndrome from Caroli disease which is more commonly from chronic inflammation from biliary stasis from cystic lesions (1). Surgical intervention of these cysts can lead to cure however does have associated morbidity and has a risk of recurrence of disease (10).

Due to location of lesions, there is a higher risk of malignant transformation to cholangiocarcinoma. Blood and/or cystic fluid aspirate test evaluations can be useful in some instances, but often are not associated with malignant potential and rather misleading in clinical practice. Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) are the most commonly tested labs but cannot be used to distinguish between benign lesions or malignant lesions (1). CA19-9 has been shown to be elevated in PLD in most cases, but does not always correlate with malignancy (7). Although this CPG discussed testing tumor markers thoroughly, there remains a lack of clarity of the usefulness in clinical practice and could have been explored more.

In regard to imaging to differentiate benign from malignant, septation within the cyst is more commonly seen in malignant cystic liver lesions and has been defined as criteria for surgical intervention; however, there is some discrepancy regarding the quality of septation with thickened walls not always indicative of malignancy (4). Nodularity or mural nodes are more commonly associated with malignant lesions as well (5). However, due to lack of evidence, EASL does not provide good recommendations for imaging to determine malignant transformation, and individuals need to develop their own management plan based on experience.

Symptom monitoring is crucial for PLD due to implications for treatment. Symptoms of abdominal pain and back pain are common due to hepatomegaly and subsequent compression on nearby organ systems of stomach and intestines from increased liver volume (9). Complex liver cysts are cysts with other features such as wall thickening, septations or variable internal fluids and are important to distinguish from simple liver cysts. Complex liver cysts are more common in patients with ADPKD and can lead to complicated cysts with hemorrhage or infection and present with symptoms of pain, fever or obstructive jaundice (8).

Cystic liver lesions, both simple and complex, have the potential to become infected or bleed in the cyst (1). General consensus agrees with antibiotic treatment for suspected infected cystic liver lesions with possibility of surgical drainage if no improvement, however more studies are needed to provide guidance on diagnosis and management in these cases (1,7). Unprovoked abdominal pain is often the first symptom and hemorrhage can occur either spontaneously in larger cysts or from trauma (1). Conservative management with observation is often preferred and reduction of bleeding risk by stopping anticoagulant medications is helpful. Differentiation of hemorrhage from malignant transformation can be difficult, but if cyst size decreases over time, is more consistent with hemorrhage which can be reassuring to monitor (5). Identification of hemorrhage can be difficult especially in patients not on anti-coagulant therapy with no increased risk of bleeding. Of note, there was no clear evidence for why certain cysts bleed and it is not a feasible trial to complete so will rely upon clinical judgment overall.

Several treatment options exist for various cystic liver lesions. They range from simple observation and no intervention, especially in the case of solitary simple hepatic cyst, to liver transplant in severe PLD with quality-of-life detriments and symptoms not controlled by other therapies (7). This CPG created a flowchart for processing and determination of treatment for PLD, however it appears generalized and should function solely as a general guideline as indicated with several other factors to be considered in individuals (1). Simple drainage of cysts often does not lead to resolution of symptoms due to high recurrence rate. Hence, treatments such as volume reduction of the cysts can prevent symptoms or

any complications from the lesion itself or its effect on the surrounding area (1). When available, sclerotherapy is added resulting in a higher rate of a reduction of decreased cystic volume in 94% of cases (6). Percutaneous sclerotherapy damages the epithelial lining of cyst and inhibits fluid reaccumulating (7). Sclerotherapy was in fact recommended in all cases of aspiration, which was consistent with other clinical studies, however risks remain present that should be discussed in more detail that was lacking in this CPG (1,6).

More invasive approaches like deroofing or fenestration of cysts are available to treat multiple lesions at one sitting (7). However, there can still be increased complications and morbidity with these procedures and a recurrence rate of 11–15% (6). Partial hepatectomy is another possible treatment but reserved for severe cases (7).

Liver transplant can be a definitive treatment for certain complex or complicated PLD but is challenged by having relatively low Model for End-Stage Liver Disease (MELD) Score. Exception points are needed for complications and symptoms to help with organ allotment for liver transplant (7). The authors emphasized that malnutrition and portal hypertension are often features which have impact on quality of life and require liver transplant evaluation (1).

In conclusion, the recent CPG developed by EASL to aid practitioners on how to approach and manage cystic liver lesions which is a highly desired concept. However, there remain a lot of inconsistencies and often judgment in clinical scenarios is based upon the individual patient and prior experience. A multi-centered consortium is needed for more longitudinal data going forward to have more defined criteria for overall management of cystic liver lesions.

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