Editorial

Tailoring stepwise treatment for Budd-Chiari syndrome: insights from the Asian Pacific Association for the Study of the Liver (APASL) consensus guidance

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Budd-Chiari syndrome (BCS) is a rare disease consisting of obstruction of the hepatic venous outflow tract, which can occur at any level ranging from small hepatic veins to the inferior vena cava (1-4). BCS can result from intravascular thrombosis or membranous obstruction of the hepatic venous outflow tract, or, less commonly, due to external compression from tumors, nodules, abscesses, cysts, or other intrahepatic lesions (1-3). The clinical presentation may be acute, subacute, or chronic, and varies from the absence of symptoms to complications of portal hypertension, cirrhosis and/or liver failure (5-8). Advances in the management of BCS have led to improvements in survival through multidisciplinary stepwise care consisting of anticoagulation, endovascular treatments, transjugular intrahepatic portosystemic shunts (TIPS), surgery and liver transplantation (1-3). There is geographic variation in both the presentation and management of BCS, with greater chronicity as well as more common involvement of the inferior vena cava in Asian nations (1,9,10); the recently published consensus guidance by the Asian Pacific Association for the Study of the Liver (APASL) provides an important perspective and timely guidance for clinicians.

The APASL consensus guidance provides comprehensive recommendations on the evaluation and management of BCS (1). The authors highlight that as an uncommon condition, the diagnosis of BCS can be missed, and recommend that its consideration in the differential diagnosis of acute and chronic liver disease especially in cases with uncertain etiology. Like other guidance documents, the APASL consensus guidance recommends diagnostic testing to assess for relevant risk factors, comorbidities, or underlying thrombophilias (1-3), including a GRADE 1 recommendation for testing of myeloproliferative disorders and other inherited or acquired thrombophilias (1). Although doppler ultrasound imaging is recommended as the initial test to diagnose BCS, cross-sectional imaging to confirm BCS and further characterize the obstruction is encouraged (1). Descriptions of several prognostic scoring systems are provided within the APASL consensus guidance, however routine clinical use of any one scoring system is not recommended (1). A detailed review of the approach to hepatic nodules, ranging from regenerative nodules to hepatocellular adenoma and carcinoma, is outlined and the authors advise as a GRADE A1 recommendation that hepatic nodules be further assessed with contrast-enhanced magnetic resonance

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imaging and that the diagnosis of hepatocellular carcinoma (HCC) be confirmed with liver biopsy (1). Screening for HCC is recommended due to the elevated risk in patients with BCS, although with the acknowledgement that the utility of imaging is limited by the clinical challenge in differentiating HCC from other benign liver lesions (1). A multidisciplinary care model for the evaluation and treatment of HCC is encouraged and is consistent with the approach described in other society guidance documents in which referral to specialized centers with expertise in the treatment of BCS is advised (1-3).

A stepwise approach to treating BCS is emphasized in the APASL consensus guidance document, and is consistent with recommendations of the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) which suggest prioritization of least invasive before more invasive options (1-4). The goals of treatment are focused on preserving liver function, improving portal hypertensive complications, and re-establishing vascular flow. Although large prospective trials for stepped management of BCS are not possible due to its uncommon nature, an example of the stepwise approach in a European center was defined as anticoagulation for all patients, with exceptions for liver failure (liver transplantation), focal hepatic vein thromboses (angioplasty), and consideration for TIPS and/or liver transplantation if other interventions are not successful (11). This is in contrast to a more individualized approach in which earlier endovascular treatment is offered, as supported by findings of a large Chinese cohort study in which one and ten-year survival was 98% and 77%, respectively (12). In the APASL consensus guidance, elements of both approaches are considered. Anticoagulation is described as first-line therapy in a GRADE A1 recommendation with vitamin K antagonists being preferred over direct-acting anticoagulants due to the availability of greater evidence (1). Hepatic vein recanalization using angioplasty and stenting is recommended as a preferred treatment for patients with short-length obstructive lesions, whereas TIPS with polytetrafluoroethylene-covered stents is recommended in those without improvement in symptoms of portal hypertension or liver function (1). Consistent with other guidance documents, surgical shunting and liver transplantation are recommended when other modalities are not effective (1). Response to treatment is defined as resolution of portal hypertensive signs and symptoms (e.g., ascites, hepatic encephalopathy, and portal hypertensive bleeding) and improvements in liver tests (e.g., normalization of liver transaminases and a decrease in total bilirubin to <1.5 mg/dL), and should be assessed at one month post-treatment (1). Unique to the APASL consensus guidance is the incorporation of liver stiffness measurement (LSM) as an additional tool to estimate the severity of hepatic congestion and assess therapeutic response (1). This is an emerging area of investigation and in some preliminary studies, variations in liver stiffness measurements have correlated with the clinical trajectory in patients who received anticoagulation and endovascular interventions (13-15). As the evidence for this practice grows, LSM may be useful to guide selection of initial and/or subsequent treatment modalities (9,13).

As an uncommon disorder, BCS requires multidisciplinary, stepwise care tailored to the individual patient. In addition to anticoagulation, management of symptoms of portal hypertension, and the treatment of underlying pro-thrombotic comorbidities, the availability of endovascular options to achieve functional hepatic venous flow through recanalization or mechanical decompression as well as TIPS and liver transplantation have improved outcomes for this heterogeneous disease. The APASL consensus guidance provides an important and timely update in the assessment and management of BCS which has significant relevance to both Asian and non-Asian clinical settings.

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