Noninvasive Assessment of Hepatocellular Carcinoma Tumor Thrombus: Is It All in Vein?

The detection of portal vein tumor thrombus (PVTT) in patients with hepatocellular carcinoma (HCC) has important implications for prognosis and treatment. Liver transplantation (LT) is contraindicated due to high rates of recurrence, and the presence of PVTT also informs the choice of locoregional therapy. PVTT and other forms of macrovascular invasion figure into most of the major staging systems for HCC.

Diagnosis of PVTT, like the noninvasive diagnosis of HCC, depends on accurate interpretation of cross-sectional imaging. The frequent occurrence of bland portal vein thrombus in cirrhotic patients, as well as the sometimes subtle imaging findings of tumor thrombus, can make this distinction difficult. Previous studies have identified imaging features associated with PVTT, including portal vein expansion, enhancement, neovascularity, and proximity to tumor. One early study found that the combination of a main portal vein diameter ≥23 mm and/or neovascularity within portal vein thrombus on computed tomography (CT) predicted PVTT with 86% sensitivity and 100% specificity. A more recent study has similarly found that enhancement of portal vein thrombus and expansion of the portal vein beyond its normal diameter on CT and magnetic resonance imaging (MRI) were both correlated with the presence of PVTT.

In this issue of *Liver Transplantation*, Sherman et al. describe a set of criteria for noninvasive diagnosis of PVTT. Their criteria, dubbed the A-VENA score, consist of 4 imaging features and 1 laboratory marker associated with PVTT. Imaging markers included thrombus enhancement, venous expansion, neovascularity, and proximity to tumor or prior treatment site. Enhancement was defined as Hounsfield units >20. The laboratory marker was measurement of serum alpha-fetoprotein (AFP), considered diagnostic if >1000 ng/dL. In the study cohort of 467 patients with HCC listed for LT, 59 patients were found to have portal vein thrombus. Of these patients, 12 had been judged to have PVTT on the basis of imaging. Reviewers retrospectively assessed the presence of the 4 imaging criteria, and AFP levels were determined from the medical record. Comparing patients with bland thrombus and tumor thrombus, the presence of 3 or more of the 5 criteria demonstrated impressive diagnostic performance: 100% sensitivity, 93.6% specificity, 80% positive predictive value, and 100% negative predictive value for the presence of tumor thrombus.

This study serves as further validation of previously identified imaging features of PVTT. It is important to note, as the authors of the study do, the absence of pathologic confirmation (biopsy of PVTT was performed in only 1 patient). The impression of the radiologist interpreting the images served as the de facto gold standard in this study, as it generally does in clinical practice. Because the imaging features of the A-VENA score still depend on a radiologist’s interpretation, it would be interesting to examine interreader agreement on the features and the agreement between experienced and novice radiologists.

A unique feature of the A-VENA score is the inclusion of the serum AFP level. This represents a departure from the traditional approach to PVTT diagnosis, which has relied on imaging. An elevated AFP is clinically useful when there is insufficient...
imaging evidence of tumor thrombus, and adding it as an additional criterion may increase the negative predictive value. In this study, patients with PVTT had significantly higher AFP levels on average than patients without PVTT. However, the absence of elevated AFP should not militate against a diagnosis of PVTT in a patient with suggestive imaging features, particularly in patients with tumors that do not produce AFP. It would be interesting to know how the other 4 markers perform without the inclusion of AFP. It would also be interesting to examine how these criteria perform in an MRI-based cohort because the vast majority (88%) of the patients in this study were examined by CT.

Despite these caveats, this study will be of interest to physicians involved in the diagnosis and management of HCC. Thrombus enhancement, venous expansion, neovascularity, and contiguity with a tumor are the principle features to keep in mind when assessing for PVTT. Although high sensitivity and negative predictive value are important, high specificity and positive predictive value are also critical since a false-positive diagnosis may preclude a potential recipient from LT. When there is high suspicion but not enough imaging evidence to achieve 100% specificity, biopsy of the portal vein thrombus can be performed.\(^4\) AFP levels and trends are therefore important to know when interpreting imaging, particularly after locoregional therapy, and high levels may prompt more careful scrutiny of subtle findings. However, a positive diagnosis of PVTT should rely primarily on imaging appearance, and if necessary, tissue sampling. Future studies should focus on extending the findings of this study to MRI as well as other imaging modalities, such as contrast-enhanced ultrasound.

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REFERENCES