Letter to the Editor

Diagnostic performance of LI-RADS in adult patients with rare hepatic tumors

Dear Editor,

Hepatobiliary cancers incorporate a large number of invasive carcinomas arising in the liver, gall bladder and bile ducts. Hepatocellular carcinoma (HCC) is the main histological type, the sixth most common cancer type and a leading cause of cancer related mortality[1,2]. Major risk factors for HCC include cirrhosis, chronic infection with HBV[3,4] or HCV[5,6] and non-alcoholic steatohepatitis[7]. HCC is one of the few tumors that can be diagnosed just by imaging alone following LI RADS criteria[8]. The main treatment strategies for early/intermediate HCC include transplant (considered curative both for HCC and for the underlying disease also in HIV coinfection[9-12]), R0 resection, ablation or TACE, while regarding advanced stage HCCs, chemotherapy is not recommended, and first line treatment options are TKIs as Sorafenib and Lenvatinib[13]. Other liver primary tumors do not share the same characteristics as HCCs.

Cholangiocarcinomas (CCA) are invasive tumors originated from the epithelium of the bile duct and can be classified according to their localization in the biliary tree as extrahepatic, more common, and intrahepatic cholangiocarcinomas[14,15]. Surgery remains the most efficient way in order to preserve the liver function. Generally, it followed by adjuvant chemotherapy, in early/intermediate cases while palliative chemotherapy with Cisplatin Gemcitabine is the recommended first line treatment in advanced types. Combined hepatocellular-cholangiocarcinomas (cHCC-CCA) are primary liver tumors with both hepatocytic and cholangiocytic differentiation[16]. CCA and cHCC-CCA need histological confirmation for diagnosis: although imaging presents malignant features, these are not specific to allow for non-invasive diagnosis. The differential diagnosis from HCC is one of the main issues in treating primary liver tumors[17]. An interesting study published by Granata et al[18] evaluated the diagnostic sensitivity and specificity of LI RADS criteria in patients with rare hepatic tumors in order to expand its use not only for HCC but also for other primary tumors that, at the moment, are still in need for biopsy. The final population included 95 patients (46 females and 49 males) with a mean age of 51 years: 83 patients had solid lesions and 12 patients had cystic lesions (simple or complex). According to radiological features, 82 patients were rated as malignant (79 true malignant, 3 false malignant) and 13 patients all rated as true benign lesions. The Liver Imaging Reporting and Data System (LI-RADS) has been developed to standardize the reporting and data gathering of liver imaging after maths in liver lesions. It is an indication of the relative risk for hepatocellular carcinoma (HCC): it assigns category codes based on imaging detected major and ancillary features[19].

The system has been developed in 2008 by a commission of radiologists, surgeons, pathologists, lexicon experts, hepatologists, and other experts. Imaging plays a very critical role in the diagnostic path of HCC in at-risk patients: it represents a non-invasive way to diagnose this tumor[20]. LI-RADS is intended only for individuals at risk for HCC (such as cirrhosis, male gender, age > 50 years, hemochromatosis, diabetes, hepatic steatosis, exposition to carcinogenic elements, alcohol abuse, obesity and the combination of several risk factors), whether or not a nodule has previously been noted by ultrasound (US) or other imaging techniques. Definite or probable benign lesions are categorized, respectively, as LR-1 and LR-2. If the characteristics of the mass suggest that it might be a malignancy other than HCC (e.g., CCA), it is categorized as LR-M (probable malignancy, not specific for HCC): unmistakable diagnosis

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requires biopsy. If there is definite tumor in a vein, whether a primary mass is clearly visible or not, the observation is categorized as malignant (LR-5V). A malignant diagnosis would thus be established, but whereas intravascular tumor is most common in HCC, it can be observed in intrahepatic cholangiocarcinoma (ICC) as well. The remaining observations are categorized LR-3, LR-4, or LR-5, based primarily on presence or absence of major features. The final category may be adjusted using ancillary features and some prespecified decision rules[21]. Granata et al[18] confirmed the diagnostic power of LI-RADS criteria allowing for differential diagnosis between benign and malignant lesions and HCC and non-HCC diagnosis, with a positive predictive value of 96.3% and a negative predictive value of 100.0%, confirming known data from literature[22]. While no significant differences were identified among LR-M categories, one of the key findings of this study is identifying some ancillary features as predictive of non-HCC specific histology: satellite nodules appeared as a characteristic feature of cHCC-CC (p value < 0.05 at Chi square test), while intralesional necrosis and hemorrhage were predictive of sarcoma (p value < 0.05 at Chi square test). Indeed, some scholars[23] support the high specificity for LI RADS to help distinguish HCC from rare non-HCC primary hepatic tumors. Although ancillary features are not mandatory, its use could potentially help in selecting those patients who would benefit from histological confirmation, since treatment options are radically different between HCC and non-HCC tumors. There are two main limitations to this study; firstly, its design: given its focus to the relatively rare non-HCC hepatic tumors, it was deemed necessary a retrospective design in order to include a larger population. For this reason, it is open to numerous biases: in the first place, the need for a pathology report may have influenced patient's selection. Since histological confirmation is not always needed in clinical practice, this could affect the report showing HCC features in non-HCC primary tumors. Furthermore, while different group of primary tumors were represented, the majority were cHCC-CCA; hence, results cannot be easily generalized. However, the long recruitment time (10 years) may have balanced this issue. Unfortunately, there is no mention of inclusion criteria in the selected population. LI-RADS criteria are recommended only for routine surveillance in at risk for HCC population (> 18 years with cirrhosis, chronic HBV infection in absence of cirrhosis, current or prior HCC), thus they are not applicable to the general population[24]. It must be kept in mind that, for example, the presence of LI RADS risk criteria can influence and alter imaging features thus increasing the chance of misclassification. For these reasons, there is no real consensus on these criteria[25].

Nevertheless, this analysis allows for more in-depth knowledge about imaging behavior of HCC and non-HCC primary tumors. Following further investigations, this will help not only in differential diagnosis between benign and malign lesion, but also in identifying by imaging alone some class of rare primary hepatic tumors, according to one of the main staples of LI RADS. Although histological confirmation remains the gold standard for non-HCC tumors, improving imaging classification will help identifying the best treatment choice in situations where biopsy may be difficult or at high risk of complications. This could also raise a relevant question: is it worth trying to revise LI RADS to assess each hepatic malignancy or is there the need for a new classification system?

Conflict of Interest

The Authors declare that they have no conflict of interests.

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