LETTER TO THE EDITOR

GB-RADS score, a possible role for CEUS?

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Dear Editor,

We read with great interest the work by Gupta and colleagues entitled "Gallbladder reporting and data system (GB-RADS) for risk stratification of gallbladder wall thickening on ultrasonography: an international expert consensus" [1]. The application of a scoring system based on qualitative features of B-mode examination to the study of gallbladder thickening is certainly a great innovation in relation to a pathology that is often not well examined and towards which there are many interpretative doubts based on low research work or evidence. As highlighted by the authors, the different categories correlate with an increasing risk of malignancy (from 1 to 5).

The category with score 0 represents an exam that cannot be interpreted or not conclusive due to confounding factors related to the patient or to the pathological state of the gallbladder itself. On the one hand, this seems to be a category that the authors included for a methodological issue, on the other it is necessary to underline that it often represents everyday life due to inadequate preparation of the patient or bowel meteorism. Furthermore, we underline that while category with score 5 is related to a gallbladder thickening at very high risk of malignancy (almost certain diagnosis) in which all the ultrasound criteria suggestive for malignancy are summarized (invasion of the surrounding tissues) with optimal diagnostic accuracy, interpretative doubts are still present on categories with score 3 or 4; indeed, the criterion of wall stratification alteration is reported in both the stages.

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In category with score 3 much emphasis is placed on the evaluation of intramural findings such as cysts or echogenic foci, which are often not clearly identifiable (sometimes the use of a high-frequency probe is used to evaluate these findings in the fundus of the gallbladder). In category with score 4 the loss of interface with the liver is the main finding, but that feature is often difficult to detect on B-mode examination if the conditions are not optimal (obesity, artifacts from meteorism). Those interpretative concerns are related to a wide variability of the risk percentage which ranges from 2 to 50% for category 3 and from 50 to 90% in category 4.

In our opinion, the use of the contrast-enhanced ultrasound (CEUS) would further improve the diagnostic performance of the score. Regarding the study of focal liver lesions and in particular of those suspected for hepatocellular carcinoma in patients with chronic liver disease, the American College of Radiology (ACR) incorporated CEUS into the Liver Imaging Reporting and Data System (LI-RADS) in 2016, due to high specificity and best diagnostic accuracy than conventional ultrasound [2, 3]. In the field of breast cancer, evaluation of lesions through the Breast-Imaging Reporting and Data System (BI-RADS) with CEUS resulted in reduced biopsy rates and increased cancer-to-biopsy yields [4]; in particular, CEUS-based characterization of BI-RADS 4A category reached sensitivity and specificity values of 85.4% and 87.8%, respectively, for the diagnosis of malignant disease [4].

Therefore, CEUS allows a better resolution of the structures and a better distinction between the gallbladder wall and the surrounding anatomical structures; moreover, there would also be an improvement in the resolution of the wall thickening towards the endocholecystic content (biliary sludge) [5, 6]. Notably, the better definition of the anatomical details allows a more specific evaluation of the invasion criterion of the surrounding tissues of the mass. Secondly, CEUS allows to optimize the resolution of those intramural findings such as cysts and anechoic spaces, which lead to a more propensity for a benign lesion. When comparing focal gallbladder adenomyomatosis with gallbladder cancer on ultrasound and CEUS, lesion iso-enhancement or hypo-enhancement,

intramural anechoic space and intactness of gallbladder wall were all signs suggestive for adenomyomatosis [7]. In particular, non-enhanced avascular Rokitansky–Aschoff sinuses could be more clearly visualized on CEUS as non-enhanced area within the thickened gallbladder wall in 83.3% of adenomyomatosis [8].

Moreover, CEUS allows to add qualitative and quantitative details that can increase the accuracy for the diagnosis of malignant lesion such as hyperenhancement in the arterial phase with subsequent washout. The malignant lesions are characterized by a "fast-in and fast-out" enhancement pattern on CEUS [9–11]; in particular, the detection of a washout time ≤ 40 s has been related to a sensitivity, specificity, and accuracy of 88.24%, 85.62%, and 86.11%, respectively, for the diagnosis of malignant gallbladder lesions [9]. In a recent work by Boddapati et al. performed on patients with gallbladder wall thickening, washout on CEUS was significantly related to malignancy ($p = 0.007$) [11]; the detection of a washout time within 53.5 s and 51.5 s was related to an area under curve (AUC) 0.927 in diagnosing malignant lesions [11]. In a previous work by Chen et al., inhomogeneous enhancement in the arterial phase was the strongest independent predictor of malignancy (odds ratio, OR 51.162), followed by interrupted inner layer (OR 19.788), washout time ≤ 40 s (OR 16.686), and wall thickness > 1.6 cm (OR 3.019) [10]. Notably, CEUS diagnostic performance (AUC = 0.917) was better than that of multi-detector computed tomography (AUC = 0.788, $p = 0.070$) in this work [10].

Since few published works and evidences, there are currently no reliable data on CEUS and metastatic lesions of the gallbladder wall [12]. There is no CEUS typical pattern for metastatic lesion due to the variability of enhancement of the structure of the lesions [12]. For example, metastasis with a large necrotic component may not have enhancement [12]. Dong et el. evaluated only two metastatic lesions in their work as hypoenhanced lesions during the late phase on CEUS [8]. Therefore, the use of CEUS actually does not allow to make a differential diagnosis between gallbladder adenocarcinoma and metastasis [12].

In conclusion, CEUS may be a low-cost, free of side effects, and fast tool that could increase the diagnostic performance of the GB-RADS score and perform a more accurate screening of which patients to submit to second-level methods such as computed tomography and/or magnetic resonance.

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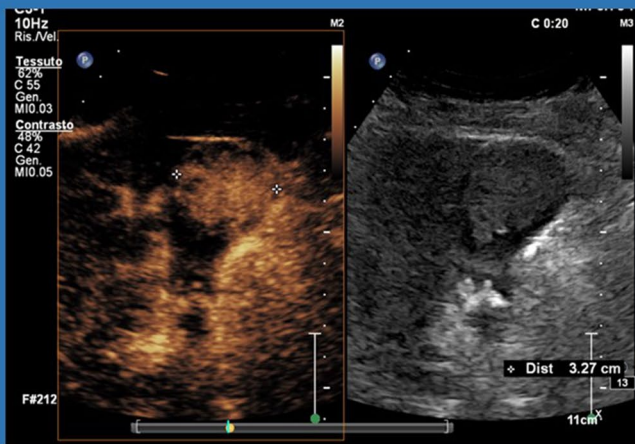
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Declarations

Conflict of interest The authors declare no conflict of interest.

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