EUS-derived criteria for distinguishing benign from malignant metastatic solid hepatic masses

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Background: Detection of hepatic metastases during EUS is an important component of tumor staging.

Objective: To describe our experience with EUS-guided FNA (EUS-FNA) of solid hepatic masses and derive and validate criteria to help distinguish between benign and malignant hepatic masses.

Design: Retrospective study, survey.

Setting: Single, tertiary-care referral center.

Patients: Medical records were reviewed for all patients undergoing EUS-FNA of solid hepatic masses over a 12-year period.

Interventions: EUS-FNA of solid hepatic masses.

Main Outcome Measurements: Masses were deemed benign or malignant according to predetermined criteria. EUS images from 200 patients were used to create derivation and validation cohorts of 100 cases each, matched by cytopathologic diagnosis. Ten expert endosonographers blindly rated 15 initial endosonographic features of each of the 100 images in the derivation cohort. These data were used to derive an EUS scoring system that was then validated by using the validation cohort by the expert endosonographer with the highest diagnostic accuracy.

Results: A total of 332 patients underwent EUS-FNA of a hepatic mass. Interobserver agreement regarding the initial endosonographic features among the expert endosonographers was fair to moderate, with a mean diagnostic accuracy of 73% (standard deviation 5.6). A scoring system incorporating 7 EUS features was developed to distinguish benign from malignant hepatic masses by using the derivation cohort with an area under the receiver operating curve (AUC) of 0.92; when applied to the validation cohort, performance was similar (AUC 0.86). The combined positive predictive value of both cohorts was 88%.

Limitations: Single center, retrospective, only one expert endosonographer deriving and validating the EUS criteria.

Conclusion: An EUS scoring system was developed that helps distinguish benign from malignant hepatic masses. Further study is required to determine the impact of these EUS criteria among endosonographers of all experience. (Gastrointest Endosc 2015;81:1188-96.)

(footnotes appear on last page of article)

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Imaging of the liver is an essential component of cancer staging because the liver is an important site of distant metastases for most tumor types.[1,2] The resulting impact on prognosis, selection of therapy, and patient outcome is substantially altered in the majority of patients with hepatic metastases.[3,4] For most cancers, the finding of hepatic metastasis indicates a noncurative status and poor prognosis with shortened survival.[3-7] The liver is most often assessed for metastases by CT or magnetic resonance

imaging (MRI). However, the accuracy of these imaging modalities for detecting hepatic masses and distinguishing benign from malignant masses is limited.[8-10] Given the impact on patient care and outcome, tissue confirmation of hepatic metastasis often is indicated.

Traditionally, and in many centers even today, percutaneous hepatic biopsy is preferred because of ease of access, reduced cost relative to EUS, and the belief that the liver cannot be well-examined or safely accessed for EUS-guided FNA (EUS-FNA). There are limited data assessing the capability of EUS for use in identifying and safely doing biopsies of hepatic masses and in understanding EUS features that discriminate benign from malignant hepatic masses.

The aim of this study was to derive and validate EUS criteria that can distinguish between benign and malignant solid hepatic masses and to determine the interobserver agreement (IOA) of these EUS features among an internationally recognized group of highly skilled endosonographers. Furthermore, we sought to examine our institutional experience with EUS-FNA of solid hepatic masses and compare EUS detection with noninvasive imaging methods.

METHODS

Patient selection

A prospectively maintained Mayo Clinic, Rochester, EUS database was reviewed to identify consecutive patients who underwent EUS-FNA of hepatic masses from January 1, 2000 through March 30, 2012. The Institutional Review Board granted study approval. Data pertaining to the clinical presentation, noninvasive imaging features, EUS findings, pathology interpretations, treatment, and patient outcomes were collected. Electronically stored images from all EUS examinations were reviewed by M.J.L, who was blinded to all details of patient medical records and did not know which patients had benign or malignant hepatic lesions. Images that corresponded to the sampled hepatic masses, as verified by the presence of an image showing an FNA needle within the mass and/or having identical dimensions to that described in the procedure note, were identified. Patients were excluded whenever the mass from which the biopsy specimen was obtained could not be confirmed and/or the available images were of insufficient quality.

DIAGNOSTIC CRITERION STANDARD

FNA interpretations were compared with a strict diagnostic criterion standard. The hepatic mass was considered malignant if within 3 months of the index EUS examination either of the following were documented: (1) Cytology and/or histology obtained from the mass was interpreted as positive for malignancy, based on material obtained via EUS, percutaneous or surgical routes, or autopsy. (2) There was a new or enlarging radiographic (CT or MRI) hepatic mass that the reporting radiologist interpreted as clearly indicative of metastasis.

The hepatic mass was considered benign when both of the following were present: EUS-FNA was interpreted as benign or negative for malignancy, and any one of the following was true: (1) No imaging before EUS, but radiographic (CT or MRI) imaging 6 months or more after the index EUS-FNA examination was interpreted as classic for a benign hepatic mass or showing no lesion. (2) Radiographic (CT or MRI) imaging before EUS showed an indeterminate hepatic mass, which on repeat radiographic imaging at 6 months or later had resolved or was seen but without enlargement, was benign appearing, and imaging showed no new hepatic masses. (3) The patient was alive, without clinical evidence of malignancy, at least 24 months after the index EUS examination.

When the findings did not satisfy the criteria for a malignant or benign hepatic mass, the results were deemed indeterminate, and the case was excluded from subsequent analysis. The EUS-FNA interpretations were compared with the strict diagnostic criterion standard to determine the number of true positive (TP), false positive, true negative (TN), or false negative results. Selection of EUS cases for the subsequent interobserver study mandated both a verifiable and representative EUS image of the sampled mass and a TP or TN FNA cytology result. The masses with predominantly cystic components were excluded. The remaining images were deidentified and separated into 2 groups consisting of 100 cases each that were matched with regard to the primary tumor site and the percentage of TP and TN results. (Appendix 1, available online at www.giejournal.org).

INTEROBSERVER STUDY OF THE INITIAL ENDOSONOGRAPHIC CHARACTERIZATION

Deidentified EUS images of the first set of 100 hepatic mass images (derivation cohort) were incorporated into a research electronic data capture (REDCap) survey. REDCap is a secure, Web-based application designed to support data capture for research studies.[11]

The first review of the derivation cohort involved completion of the REDCap survey by 10 expert endosonographers who were blinded to all clinical and cytopathology information, each using a unique password. In addition to rating 15 EUS features of each lesion, the reviewers provided their opinions as to whether the mass was benign or malignant. The 15 questions addressed potentially predictive features that were chosen based on their use when other structures at EUS were being described and based on the clinical experience of endosonographers and sonographers within our institution doing noninvasive procedures.