Diagnosis and management of GI stromal tumors by EUS-FNA: a survey of opinions and practices of endosonographers

Christina Y. Ha, MD, Rajesh Shah, MD, Jaijing Chen, MPH, Riad R. Azar, MD, Steven A. Edmundowicz, MD, Dayna S. Early, MD

St Louis, Missouri, USA

Background: There is no consensus regarding the best management strategy for diagnosing and treating GI stromal tumors (GISTs).

Objective: Our purpose was to examine the practice patterns of endosonographers in diagnosing and managing GISTs, particularly features of GISTs suggestive of malignancy, features that prompt surgical referral, and surveillance patterns.

Design: An invitation to complete an online survey was e-mailed to all 413 members of the American Society for Gastrointestinal Endoscopy EUS Special Interest Group.

Results: A total of 134 (32%) members responded; 59% of respondents use EUS features combined with FNA findings to diagnose GIST, and 89% consider a *c-kit*–positive stain on FNA most suggestive of GIST. However, 60% would diagnose GIST when cytologic samples are insufficient for diagnosis, and 40% would diagnose GIST if cytologic samples are sufficient but *c-kit* is negative. A total of 92% use size as the main criterion to distinguish benign from malignant GISTs, and 90% refer lesions >5 cm for surgery. For lesions not resected, 70% survey annually, 19% less than annually, 10% more than annually, and 1% do not survey.

Limitations: The opinions of the respondents do not necessarily reflect the opinions and practices of endosonographers nationwide. There are inherent limitations to an online multiple-choice survey, including low response rates.

Conclusions: There are substantial practice variations in diagnosing, resecting, and surveying GISTs. A majority of our survey respondents have made the diagnosis of GIST without FNA confirmation. Size >5 cm is the feature used most to predict malignancy and to prompt surgical referral. Surveillance practices for unresected GISTs are variable. Evidence is needed to establish practice guidelines in this area. (Gastrointest Endosc 2009;69:1039-44.)

GI stromal tumors (GISTs) are the most common mesenchymal tumors of the GI tract, are often discovered incidentally during routine upper endoscopy, and are a frequent indication for referral for endosonography. GISTs typically arise from the muscularis propria and are hypothesized to originate from the interstitial cells of Cajal. A majority of GISTs abnormally express a specific tyrosine kinase receptor *(c-kit)* leading to a gain-of-function mutation associated with unregulated cell growth.[1-4]

Abbreviations: AGA, American Gastroenterological Association; ASGE, American Society for Gastrointestinal Endoscopy; GIST, GI stromal cell tumor; SIG, special interest group.

DISCLOSURE: *All authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
doi:10.1016/j.gie.2008.07.041

EUS plays an important role in the characterization of subepithelial lesions by providing information about their layer of origin, echogenicity, size, and local invasion. Endosonographically, GISTs appear as solid hypoechoic masses arising from the second or fourth sonographic layer of the GI wall.[5-7] Although the endosonographic appearance of a lesion may suggest a GIST, tissue is necessary to confirm the diagnosis. Several groups have recently reported success with EUS-guided FNA in the evaluation of suspected GISTs. These studies demonstrated that combining FNA cytologic examination with immunohistochemical analysis for *c-kit* can accurately diagnose GIST.[8-12]

The primary purpose of EUS evaluation of submucosal lesions is to determine whether the lesion is truly a GIST. Miettinen et al[13] predict the overall incidence of malignant GISTs to be 20% to 30% of all soft-tissue sarcomas. A recent endosonographic case series found 11% of analyzed GISTs to be malignant, with an additional 19% of examined

GISTs to be ''borderline,'' defined as GISTs of indeterminate malignant potential. However, these numbers may reflect an overestimation of the true malignant potential of GISTs because only lesions verified by pathologic examination were included.[14] The National Institutes of Health risk stratify the malignant potential of GISTs on the basis of the number of mitotic figures per high-power field and size.[15] A pitfall of EUS-FNA is that it cannot consistently and accurately differentiate benign from malignant GISTs because mitotic activity is often not seen on smears. The only way to definitively assess malignant potential of GISTs is through surgical excision. Size >3 to 5 cm appears to be the only preoperative criterion that reliably predicts the malignant potential of GISTs and the postoperative survival.[16-19] However, smaller-sized GISTs have also been reported to undergo malignant transformation with metastases.[12] A recent American Gastroenterological Association (AGA) technical review of gastric subepithelial lesions recommended that a cutoff value of 3 cm be used to determine whether surgical resection is indicated for an asymptomatic GIST, although this recommendation was based on expert opinion only.[20] There is currently no consensus regarding the best management strategy for small (asymptomatic) GISTs.

The aim of our study was to examine the practice patterns of endosonographers in diagnosing and managing GISTs. We hypothesized that, despite published guidelines regarding the management of GISTs, there would be substantial variation in practice patterns regarding the EUS and FNA features of GISTs, the features suggestive of malignancy, the features that prompt surgical referral, and surveillance patterns.

Capsule Summary

What is already known on this topic

- GI stromal tumors (GISTs) are often discovered incidentally during routine upper endoscopy and are a frequent indication for referral for endosonography to obtain information about origin, echogenicity, size, and local invasion.

What this study adds to our knowledge

- In a survey of 134 sonographers, most have made the diagnosis of GIST without FNA confirmation, and size >5 cm is the feature used most to predict malignancy and prompt surgical referral.
- Surveillance practices are highly variable.

METHODS

Subjects

E-mail invitations were sent to all members (413 at the time) of the American Society for Gastrointestinal Endoscopy (ASGE) EUS Special Interest Group (SIG) to participate in an anonymous online survey with questions focusing on diagnosis, surgical referral, and surveillance of GISTs. Initial nonresponders received a second e-mail invitation to complete the survey.

Survey

The 13-question survey was conducted by using an online survey tool (Appendix 1, available online at www.giejournal.org). In the first part of the survey, participants were asked to describe their practice settings, referral populations, and number of subepithelial lesions evaluated the month before survey completion. The second part of the survey evaluated endosonographers' opinions regarding EUS and FNA features suggesting a diagnosis of GISTs and EUS and FNA features suggestive of malignant GISTs. The final part of the survey examined endosonographers' practice patterns regarding surgical referral and EUS surveillance of GISTs. Respondents were asked to choose answers from multiple choices relevant to each question.

Although this survey was not formally validated for data collection, the survey was reviewed independently for content and format of the questionnaire by 3 expert gastroenterologists at 3 different institutions who routinely perform EUS. Additionally, the design of the study was a simple multiple-choice response. Skipped questions were not included in the overall response totals. For the entire survey, there was a 90% or higher response rate for each question. The Washington University School of Medicine Human Research Protection Office approved the study.

Statistical considerations

Descriptive statistics were used to summarize the responses of the survey, including participant characteristics and clinical questions. Percentages were calculated and used for display in the figures. Proportions of the responses were compared between private practice and academic groups with the χ^2 test, with Yates' correction for continuity where appropriate. We considered a P value less than .05 as statistically significant. It is recognized that there was multiple testing of outcome data arising from individual respondents. The uncorrected P values are presented along with the effect of correction by the method of Bonferroni whenever that correction would remove statistical significance at the $P < .05$ level. Analysis was carried out by use of SAS 9.1 (SAS Institute, Cary, NC).

RESULTS

Of the 413 invitations to participate, 134 (32%) endosonographers responded. The demographics of the respondents are shown in Table 1. Among the 134 gastroenterologists who responded to the survey, 77% performed EUS of more than 2 subepithelial lesions in