Low-grade dysplasia diagnosis ratio and progression metrics identify variable Barrett's esophagus risk stratification proficiency in independent pathology practices CME

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Background and Aims: The diagnosis of low-grade dysplasia (LGD) in Barrett's esophagus (BE) is subject to substantial interobserver variation. Our central aim in this study is to compare independent pathology practices using objective measures of BE risk stratification proficiency, including frequency of diagnosis and rate of progression, with high-grade dysplasia (HGD) or adenocarcinoma (EAC) after the first diagnosis of LGD.

Methods: We retrospectively evaluated over 29,000 endoscopic biopsy cases to identify 4734 patients under endoscopic biopsy surveillance for BE in a healthcare system with multiple independent pathology practices: a subspecialized GI pathology group (SSGI; 162 BE cases per pathologist annually), 3 high BE volume general surgical pathology practices (GSPs; >50 BE cases per pathologist annually), and multiple low BE volume GSPs (10.6 BE cases per pathologist annually). We measured LGD diagnosis frequencies and rates of diagnostic progression to HGD or EAC in patients diagnosed with LGD.

Results: The proportion of all BE cases diagnosed as LGD (LGD/BE diagnosis ratio) ranged from 1.1% to 6.8% in the different hospital settings ($P < .001$). The cumulative proportion of patients with HGD or EAC within 2 years of the first diagnosis of LGD was 35.3% in the SSGI and ranged from 1.4% to 14.3% in the GSPs ($P < .001$). LGD diagnosed by the GSP with the lowest LGD/BE diagnosis ratio had an adjusted risk of progression similar to LGD diagnosed by subspecialists (hazard ratio, .42; 95% CI, .06-3.03). However, when LGD was diagnosed by other generalists, the adjusted risk of progression was 79% to 91% lower than subspecialists ($P < .001$). When LGD was diagnosed in a low-volume GSP practice, the risk of progression was not significantly increased relative to patients with nondysplastic BE (hazard ratio, 1.3; 95% CI, .4-3.9).

Conclusions: General surgical pathologists and subspecialists show highly significant differences with respect to LGD/BE ratio, risk of progression relative to nondysplastic BE, crude annual progression rates, and the cumulative 2-year progression rate after LGD. These metrics can be used to assess proficiency in BE risk stratification in historical cases. Some general practitioners were able to achieve results similar to subspecialists. General surgical pathologists with little annual experience evaluating BE biopsy specimens did not successfully risk stratify patients with BE. (Gastrointest Endosc 2018;88:807-15.)

Abbreviations: BE, Barrett's esophagus; EAC, esophageal adenocarcinoma; GSP, general surgical pathology practice (high annual volume of Barrett's cases); HGD, high-grade dysplasia; IFD, indefinite for dysplasia; LGD, low-grade dysplasia; LV-GSPs, low volume general surgical pathology practices (low annual volume of Barrett's cases); SSGI, subspecialized GI pathology practice.

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Barrett's esophagus (BE) has a disquieting reputation as the primary risk factor for esophageal adenocarcinoma (EAC), but in absolute terms, it confers a cancer risk of less than .5% annually for adults.[1] Endoscopic biopsy specimens are used to guide surveillance and treatment decisions based on the relative risk of developing cancer associated with different grades of dysplasia. Patients with high-grade dysplasia (HGD), facing a 5% to 8% annual incidence of EAC, are recommended to undergo definitive treatment and complete eradication of the BE segment.[2,3] Patients with nondysplastic BE are followed at 3- to 5-year intervals, reflecting its low .3%, annual incidence of EAC.[4,5]

For patients diagnosed with low-grade dysplasia (LGD), the annual incidence of EAC is estimated at .5% and the annual incidence of HGD or EAC is estimated at 1.7%, with individual studies ranging from 0% to 13.4%.[3,6,7] Multiple factors may contribute to variability of reported outcomes after a diagnosis of LGD: small number of patients with LGD in some studies, failure to differentiate prevalent from incident progression, referral bias, and limited follow-up data.[8] Perhaps the most significant underlying factor is the imprecision of diagnostic criteria used to differentiate regenerative epithelial atypia from epithelial dysplasia on 1 end of the spectrum and to differentiate LGD and HGD on the other end of the spectrum.[9] The accepted criteria describe an array of cytologic and architectural features that combine to form a continuum of atypia that at some point, individually or cumulatively, indicate "neoplastic transformation" has occurred.[10,11]

Interobserver disagreement on the diagnosis of LGD has been well chronicled.[10-21] Studies with centralized pathology review by pathologists practicing in academic institutions reveal low rates of agreement with general surgical pathologists who practice in nonacademic/community hospital settings.[13-15,17,18,22,23] In these reports, study pathologists confirm the diagnosis of LGD in only 15% to 63% of cases, with downgrades of LGD the most common outcome after review. Overdiagnosis of LGD should result in low rates of progression, as suggested by a meta-analysis that showed a negative correlation between the proportion of patients with LGD in a study and the study's reported rate of progression from LGD to EAC.[4]

Based on these findings, it is recommended that all LGD BE diagnoses be submitted for confirmatory review by at least 1 expert GI pathologist (defined as "a pathologist with a special interest in BE-related neoplasia and who is recognized as an expert in this field by his/her peers").[2,3,6] Although this is a reasonable recommendation, reliance on a purely subjective definition of expertise may limit the strategy's effectiveness because experts often disagree with one another on BE dysplasia grade when blinded to the opinions of their peers.[11,12,16,20] Consultants, consequently, are encouraged to self-audit and report the proportion of BE cases diagnosed with LGD (LGD/BE ratio) as well as relative rates of neoplastic progression among patients diagnosed with LGD versus nondysplastic BE.[6]

The aim of this study is to compare multiple, independent pathology practices using several diagnostic performance metrics, including LGD/BE diagnosis ratio, relative risk of neoplastic progression in patients diagnosed with LGD versus nondysplastic BE, crude annual progression rates, and 2-year cumulative progression. We relate these performance metrics to characteristics of the practices (subspecialist/generalist and annual BE case volume).

METHODS

This study was a retrospective review of all esophageal and gastroesophageal junction biopsies performed at the University of Pittsburgh Medical Center affiliated hospitals. It was approved by the University of Pittsburgh Institutional Review Board (PRO15080138).

Biopsy specimen classification

We searched the centralized pathology database used by all hospitals in the system for esophageal and gastroesophageal junction biopsy specimens for suspected BE with histologically confirmed intestinal metaplasia. The set of biopsy specimens from the esophagus and/or gastroesophageal junction taken at a single endoscopic examination are referred to as a "case." We recorded several attributes for each case: date of the procedure, hospital that rendered the diagnosis, and highest grade of dysplasia (nondysplastic BE, indefinite for dysplasia [IFD], LGD, HGD, EAC). Cases reviewed by the subspecialized center in consultation were assigned to the subspecialized center if the diagnosis was made within 90 days of the endoscopic procedure. Cases referred from outside the University of Pittsburgh Medical Center system in consultation were assigned to the hospital where the diagnosis was made. All other (routine) cases were assigned to the hospital where the diagnosis was originally made.

Patient classification and follow-up

Each patient was categorized based on the highest grade of neoplasia during surveillance (nondysplastic BE, IFD, or LGD). We defined "surveillance" cases as those obtained during the time period from the index endoscopic procedure to last endoscopic procedure for patients never diagnosed with HGD/EAC. For patients diagnosed with HGD or EAC, surveillance cases included the index case and all cases that preceded the first diagnosis of HGD or EAC. We recorded the hospital where diagnoses were made for each patient. Approximately 20% of patients had diagnoses from more than 1 hospital during surveillance. For these, we recorded the hospital where the highest grade of dysplasia was first diagnosed during surveillance. To illustrate, for patients diagnosed with LGD during surveillance, we recorded the hospital that assigned the first LGD diagnosis, whereas patients diagnosed with IFD during surveillance but not LGD were assigned to