Barrett’s Esophagus With Low-Grade Dysplasia: Ablate or Wait?

Sravanti Parasa, MD1 and Prateek Sharma, MD2

Am J Gastroenterol advance online publication, 24 January 2017; doi:10.1038/ajg.2016.605

INTRODUCTION
Barrett’s esophagus (BE) is the only known precursor to esophageal adenocarcinoma (EAC) (1). Malignant progression in BE is thought to be a multi-step process, which develops through subsequent grades of dysplasia classified as non-dysplastic BE, low-grade dysplasia (LGD) and high-grade dysplasia resulting in cancer (1).

LGD has been shown to be a risk factor for developing high-grade dysplasia or EAC in patients with BE and these patients are recommended intensified surveillance every 12 months or undergo endoscopic ablation if eligible (2). However, controversies exist in the diagnosis and management after initial biopsy of the BE segment showing LGD. Prior studies have shown significant variability in the malignant progression rates for BE patients with LGD from 0.6% up to 13.4% (3), ambiguity of diagnosing dysplasia, the uncertain effectiveness and durability of ablation to maintain remission from metaplasia and dysplasia and prevent cancer (4).

Hence, gastroenterologists are often fraught with a dilemma as to how to manage patients who are diagnosed with LGD arising from BE. This article focuses on providing a practical framework on how these patients should be approached.

GENERAL GUIDANCE
Though recent research into objective biological markers for progression appears promising, current surveillance and treatment decisions are solely based on a conventional histopathological assessment of biopsies (5). Hence, we recommend the following steps before committing to treatment options for LGD.

Step 1: Confirming the diagnosis of LGD in BE: the 3Rs
Re-look: When confronted with an initial diagnosis of LGD, always ensure that a higher-grade area has not been missed. Was there a visible lesion? Were there any subtle abnormalities within the BE segment? Was adequate time spent inspecting the BE mucosa? A careful inspection with longer inspection times of the esophagus during endoscopy can increase the detection rates of neoplastic lesions in BE. All these factors should be kept in mind during the re-look endoscopy. In addition, a wide variety of enhancements to endoscopic imaging with white light endoscopy have been developed and studied in recent past to allow for detailed inspection of the surface (Figure 1). Both dye spray and electronic chromoendoscopy allows for detailed imaging of the mucosal and vascular surface patterns in BE. A recent meta-analysis also suggests that electronic chromoendoscopy may increase detection of dysplasia (6).

Re-biopsy: After a detailed and close inspection of the BE segment, targeted sampling of any nodularity, ulceration, erosions, plaque, stricture, or luminal irregularity in the BE segment should be performed. This should be followed by a systematic biopsy protocol with four quadrant biopsies from every 1 cm of the BE segment.

Review with experienced pathologist: A common problem in the histopathological diagnosis of LGD is the high intra and interobserver variation in the diagnosis. In a study of experienced academic pathologists, by Montgomery et al. (7), the kappa value for a diagnosis of LGD was 0.32.

Recent data emphasizing the importance of the confirmation of the diagnosis of LGD comes from two recent European studies. Upon review by two pathologists with extensive experience in the diagnosis of BE-related neoplasia, of the 147 patients diagnosed with LGD in the community, 85% were downgraded to a diagnosis of no dysplasia (3). In another study by Kestens et al., among the 10% of patients (n=161) in the study cohort in whom confirmation of LGD was established, 51% had no dysplasia at the first follow-up endoscopy, and 30% had persistent LGD. The incidence of EAC was 2.51/100 person-years (95% confidence interval, 1.46–3.99/100 person-years), in the confirmed LGD cohort compared
**Step 2: Treatment vs. surveillance**

**Ablation vs. surveillance:** Data from a multicenter randomized trial comparing radiofrequency ablation (performed by experts) with endoscopic surveillance in patients with LGD (diagnosed by local pathologist and confirmed by expert pathologist) showed that the risk of progression to EAC at the termination of study (median followup of 36 months) was 1.5% in the RFA arm compared with 8.8% in the surveillance group (9). However, it should be advised that the rate of progression of LGD to EAC in the surveillance arm is much higher compared with other studies (8.8 vs. 0.54% in a recent meta-analysis (10)). Based on the data from this RCT, endoscopic therapy appears safe and effective, but given risk of progression and recurrences after ablation, surveillance should still be continued in these patients. Data from this study should be interpreted with caution as these rates of progression are based on LGD diagnosis by expert pathologists and ablation performed by expert endoscopists.

*In patients with confirmed and persistent LGD and no life limiting illness (major co morbidities), endoscopic therapy should be performed by an expert. If closer surveillance is the preferred option due to underlying health conditions or patient preference, surveillance should be performed every 12 months.*

**Other management pointers for patients undergoing surveillance**

(a) Proton pump inhibitors should be used in patients with LGD when there are continued GERD symptoms, endoscopic and/or histological evidence of esophagitis. The dose of PPI should be titrated to resolve these issues.

(b) Routine pH monitoring in these patients is not recommended.

(c) No randomized controlled data exists to support any role of ASA/NSAIDs to prevent progression to EAC, although epidemiological evidence does indicate a negative correlation between ASA/NSAID use and EAC. Hence, routine use of ASA/NSAIDs only for this purpose is not recommended.

**Summary**

The first step in the management of BE patients with LGD is to ensure that the diagnosis is confirmed and persistent; follow the 3Rs.

1. Re-look
2. Re-biopsy
3. Review

The second step in the management of BE patients with confirmed and persistent LGD is to decide between endoscopic ablation vs. surveillance based on available endoscopic expertise and patient preference.

**CONFLICT OF INTEREST**

Guarantor of the article: Prateek Sharma, MD.

Specific author contributions: Dr Sravanthi Parasa—drafting the manuscript and has approved the final draft submitted. Dr Prateek Sharma—drafting the manuscript and has approved the final draft submitted.

Financial support: None.

Potential competing interests: None.

**REFERENCES**


---

**Figure 1.** Algorithm: Diagnosis and management of LGD in BE.

<table>
<thead>
<tr>
<th>Step 1 Confirming diagnosis</th>
<th>Step 2 Management plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm and persistent LGD</td>
<td>Assess candidacy for endoscopic treatment</td>
</tr>
<tr>
<td>No LGD</td>
<td>Ablation by expert</td>
</tr>
</tbody>
</table>

---

**Algorithm: Diagnosis and management of LGD in BE.**

- **Step 1:** Confirming diagnosis
  - Re-look
  - Re-biopsy
  - Review
  - Initial diagnosis of low grade dysplasia
  - Follow the 3Rs

- **Step 2:** Surveillance
  - Surveillence every 3–5 years
  - Annual surveillance
  - Ablation by expert
  - Annual surveillance