

LGD: surveillance or ablation?

This text is supplementary to the section entitled “LGD: surveillance or ablation?” (page 26) in the recently published BSG guidelines for the management of Barrett’s oesophagus (BO) [1]. This has come about because of newly published data on the natural history of low grade dysplasia (LGD) as well as the randomized controlled trial (RCT) on radiofrequency ablation (RFA) for this group of patients. These data have led to a new recommendation from NICE [2] and the clinical implications are important enough that the oesophageal section of the British Society of Gastroenterology feels that we should not delay a formal recommendation until the next iteration of these guidelines, which will not be issued for several years.

With regards to the diagnostic accuracy and risk of progression in patients with LGD, Duits and collaborators have conducted a large retrospective analysis of 293 patients with LGD diagnosed in community hospitals, which builds on their previous data [3, 4]. They found that, following consensus review, the original diagnosis of LGD was confirmed in just over a quarter of cases (27%) whereas the rest were downgraded. Patients with confirmed LGD had a progression rate to HGD or cancer of 9.1%/year over a median follow up of 39 months. By contrast, patients whose diagnosis was down-staged to either non dysplastic BO or indefinite for dysplasia had a conversion rate of 0.6% and 0.9%/year (Evidence grade III). This study reiterates the difficulty in making a pathological diagnosis of LGD, but also shows that when this diagnosis is confirmed by an expert pathologist from a different institution the risk of progression to HGD or cancer is substantially increased. In keeping with this, a recent meta-analysis found that studies with low LGD/non dysplastic BO ratios (<0.15), indicative of a more stringent diagnostic criteria for dysplasia, reported a significantly higher annual incidence of cancer (0.76%, 95% CI, 0.45%-1.07%) compared to studies with a ratio >0.15 (0.32%; 95% CI, 0.07%-0.58%) [5].

With regards to whether treatment should be performed in patients with LGD a recent multicentre RCT compared the outcome of 68 patients treated with RFA with an equal number of patients undergoing annual endoscopic surveillance [6]. The authors found that over a 3 year follow up period, 26.5% of patients on surveillance progressed to HGD or cancer, compared with only 1% in the treatment arm ($p < 0.001$) (Evidence grade Ib). Complete eradication of dysplasia and intestinal metaplasia were achieved in 98 and 90%, respectively, in the treatment arm and 28 and 0%, respectively, in the surveillance arm ($p < 0.001$). The most common complication was stricture, which occurred in 12% of patients, but this was successfully managed in all patients with pneumatic dilatation. These results show that RFA is safe in patient with LGD and significantly reduces the risk of progression to HGD or cancer. It should be noted that for the patient to be eligible for inclusion in this study the diagnosis of LGD had to be confirmed by a central pathologist with extensive experience in BO. It is also interesting that in 28% of patients randomized to the surveillance arm, the LGD was no longer found during the following 3 years. The most likely explanation for this is sampling error, however one cannot exclude that focal LGD could have been eradicated by biopsy.

Overall from the previous literature review [1] taken together with these new published data, we conclude that endoscopic ablation, preferably with RFA, is an appropriate treatment to offer for patients with confirmed LGD. Due to the considerable diagnostic difficulties, confirmed LGD should be interpreted as that diagnosed on at least two endoscopies and confirmed by a second expert GI pathologist. If possible the pathology review should be conducted at an external institution.

Management should be discussed at the upper GI multi-disciplinary team (MDT) meeting to ensure that the pathology review is robust and to discuss whether the patient is fit enough to consider endoscopic treatment. As noted in the current guidelines p53 immunohistochemistry can be a useful diagnostic adjunct. Hence the revised recommendation is now:

Patients with LGD should have a repeat endoscopy in 6 months time. If LGD is found in any of the follow up OGDs and is confirmed by an expert GI pathologist, the patient should be offered endoscopic ablation therapy after review by the specialist MDT. If ablation is not undertaken, 6-monthly surveillance is recommended (*Recommendation grade A for endoscopic therapy and C for surveillance*). (A+ 56%, A 33%, D 11%)

1. Fitzgerald, R.C., et al., *British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus*. Gut, 2013.
2. NICE, *Endoscopic radiofrequency ablation for Barrett's oesophagus with low -grade dysplasia or no dysplasia*. <http://www.nice.org.uk/guidance/IPG496/chapter/1-Recommendations>, 2014.
3. Duits, L.C., et al., *Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel*. Gut, 2014.
4. Curvers, W.L., et al., *Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated*. Am J Gastroenterol, 2010. **105**(7): p. 1523-30.
5. Singh, S., et al., *Incidence of esophageal adenocarcinoma in Barrett's esophagus with low-grade dysplasia: a systematic review and meta-analysis*. Gastrointest Endosc, 2014. **79**(6): p. 897-909 e4; quiz 983 e1, 983 e3.
6. Phoa, K.N., et al., *Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial*. JAMA, 2014. **311**(12): p. 1209-17.