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Radiofrequency ablation is associated with decreased neoplastic progression in patients with Barrett's oesophagus and confirmed low-grade dysplasia

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Philip Hendy reviewing Small *et al.*¹

This retrospective cohort study comparing radiofrequency ablation with surveillance in Barrett's oesophagus with confirmed low-grade dysplasia adds real clinical practice data to the recent randomised control data, and its results are in concordance with the recent change in British Gastroenterology Society guidelines.

Oesophageal adenocarcinoma (OAC) has a high mortality rate and an increasing incidence. Barrett's oesophagus (BO) is a recognised precursor of OAC. Dysplasia in Barrett's tissue is the most potent prognosticator of progression from BO to OAC. In BO with either high-grade dysplasia (HGD) or OAC confined to the mucosa, there is clear evidence that endoscopic eradication of the Barrett's mucosa reduces progression to OAC and is superior to both surveillance and surgical oesophagectomy. This practice is recommended in national society guidelines.² It is less clear what the optimal strategy to manage BO with low-grade dysplasia (LGD) is. This lack of clarity is due to the conflicting data regarding progression rates of LGD to HGD and OAC. A low rate of progression would favour a surveillance strategy, while a high rate would favour an interventional strategy with effective endoscopic therapy such as radiofrequency ablation (RFA). Early publications reported low rates of progression from LGD to HGD and OAC (1.8–2.7%³), while

more recent studies have suggested a progression rate of 11.8–14%.⁴ This difference is likely to be due to a reduction in the reported rates of LGD in the initial samples as a result of increased stringency of diagnostic criteria applied. More recent studies have utilised two regional specialist histopathologists to confirm the diagnosis of LGD, and many cases that might have been included in previous studies as LGD have been downgraded (up to 85%).⁴ A recent randomised controlled trial (RCT) showed that, in patients with BO and LGD, RFA was safe and resulted in a reduced risk of neoplastic progression over 3 years.⁵ The aim of the study reviewed here is to add 'real-world' clinical data to the evidence base examining whether RFA or surveillance is preferable for patients with BO and LGD.

The patients were recruited to this cohort study from three centres within the 'Barrett's Esophagus Translational Research Network'. The inclusion criteria were: age >18; histologically confirmed LGD (by a regional specialist histopathologist) on a background of BO within the dates October 1992 and December 2013; the subject had undergone routine endoscopic surveillance or had RFA after the diagnosis of LGD was made. The study included a period before RFA was available (pre-2006). Exclusion criteria included: prior diagnosis of HGD or OAC; prior oesophageal surgery or endoscopic therapy for BO. The surveillance group

comprised all patients identified with LGD who had at least one surveillance endoscopy after diagnosis, while the ablation cohort included all patients who underwent RFA after diagnosis. Because this was a retrospective study, the time to surveillance endoscopy or RFA was not standardised, but was less than a year in all cases.

Histological assessment was usually performed by one histopathologist experienced in BO and dysplasia. In cases of uncertainty, a second expert review was performed, and in cases of dispute, a third expert opinion was sought. The study end point was a diagnosis of HGD or OAC made during follow-up. Surveillance started either at the time of the first surveillance endoscopy or at the time of the first endoscopy with RFA.

A total of 170 patients were included, of whom 45 underwent RFA and 125 underwent surveillance only. Baseline characteristics, including baseline Barrett's segment characteristics, were similar between the two cohorts. Differences included: a higher frequency of endoscopies performed in the RFA group due to the surveillance follow-up after RFA ($p<0.001$); and a higher prevalence (non-significant $p=0.45$) of visible nodularity in the surveillance group (10.4%) than the RFA group (6.6%).

In the surveillance group, 36 (28.8%) had neoplastic progression with 29 developing HGD, 5 developing intramucosal OAC and 2 developing submucosal OAC;

corresponding to an annual neoplasia progression rate of 6.6%. There was a significantly reduced rate ($p=0.02$) of neoplastic progression in the RFA cohort with one of the 45 patients (2.2%) developing intramucosal OAC; corresponding to an annual neoplastic progression rate of 0.77%. Upon univariate analysis of the surveillance group, it was Barrett's segment length, nodularity, persistent LGD and multifocal dysplasia, which were all associated with progression to HGD/OAC. The presence of nodularity and multifocality of dysplasia were also independent predictors of neoplastic progression in multivariate analysis. Exclusion of those cases with nodularity or multifocal dysplasia did not change the primary study outcome, nor did the exclusion of patients recruited pre-2006 (when RFA was unavailable).

The authors acknowledge a number of study weaknesses including: lack of applicability to community settings (all patients in the study were referred patients at experienced referral centres); the lack of a second histopathologist to examine the samples in the majority of cases; and the difference between frequencies of surveillance endoscopies in the two cohorts.

The study concludes that endoscopic ablation has potential benefit over surveillance in the

management of patients with BO and LGD.

Comment

This is a relevant and timely publication. The British Society of Gastroenterology (BSG) recently published a supplementary update entitled 'LGD: surveillance or ablation' to add to its guidelines on the diagnosis and management of BO.² The BSG advised that, in the case of LGD in BO, rather than the previous guideline of surveillance, a second-look endoscopy should be performed at 6 months to confirm the diagnosis of LGD, and that, in confirmed cases, RFA should be performed. This change in guidance was in response to the RCT mentioned earlier, which showed a clear benefit to RFA over surveillance.

It is this editor's opinion that a second-look endoscopy (as per BSG guidance) to confirm LGD is warranted, given the difficulty associated with diagnosing LGD histologically (up to 85% downgraded to BO without dysplasia in one study).⁴ The use of a second histopathologist to confirm LGD would have improved this study, but the lack of this is not a fatal flaw. Similarly, the discrepancy between the number of endoscopies performed in the two cohorts probably did not affect outcomes, given that the median number of endoscopies performed in the 3 years of

follow-up in the surveillance cohort was still five (compared with nine in the RFA group). This study adds to the weight of evidence favouring treatment with RFA in patients with confirmed LGD over surveillance alone.

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Competing interests None declared.

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