Expert Review of Gastroenterology & Hepatology

ISSN: 1747-4124 (Print) 1747-4132 (Online) Journal homepage: informahealthcare.com/journals/ierh20

Advanced endoscopic therapeutics in Barrett's neoplasia: where are we now and where are we heading?

Gaius Longcroft-Wheaton & Pradeep Bhandari

To cite this article: Gaius Longcroft-Wheaton & Pradeep Bhandari (2015) Advanced endoscopic therapeutics in Barrett's neoplasia: where are we now and where are we heading?, Expert Review of Gastroenterology & Hepatology, 9:5, 543-545, DOI: 10.1586/17474124.2015.1034691

To link to this article: https://doi.org/10.1586/17474124.2015.1034691

Published online: 08 Apr 2015.

Advanced endoscopic therapeutics in Barrett's neoplasia: where are we now and where are we heading?

Expert Rev. Gastroenterol. Hepatol. 9(5), 543–545 (2015)

Gaius Longcroft-Wheaton

Author for correspondence: Portsmouth Hospitals NHS trust, Queen Alexandra Hospital, Southwick Hill Road, Cosham, PO63LY, UK
and
Department of Pharmacy and biomedical sciences, University of Portsmouth, Winston Churchill Avenue, Portsmouth, PO1 2UP, UK
gaius@gaius.wanadoo.co.uk

Pradeep Bhandari

Portsmouth Hospitals NHS trust, Queen Alexandra Hospital, Southwick Hill Road, Cosham, PO63LY, UK
and
Department of Pharmacy and biomedical sciences, University of Portsmouth, Winston Churchill Avenue, Portsmouth, PO1 2UP, UK

Over the last 10 years, there have been considerable changes in how we manage Barrett's neoplasia, with the shift away from conventional surgery and moving toward endotherapy for treating dysplasia and early cancer. In this editorial, we will review these changes and look forward to the possible developments which may occur over the next decade.

The last 10 years has witnessed significant changes in the examination and management of Barrett's neoplasia. Where it was previously believed that dysplastic changes were invisible, the advances in endoscopic techniques and technology has made it possible to detect and localize early neoplasia in Barrett's esophagus. This has opened up a wealth of therapeutic options, such that there has been a complete shift away from the surgical treatment of high-grade dysplasia (HGD) and early mucosal cancer toward endoscopic therapy. Endotherapy is the recommended treatment of HGD by the American Society for Gastrointestinal Endoscopy [1] and is the preferred treatment over esophagectomy in the recently updated British Society of Gastroenterology guidelines [2].

There are now several endoscopic techniques for treating neoplasia within Barrett's neoplasia. These can broadly be divided into endoscopic resection (ER), using either piecemeal endoscopic mucosal resection (EMR) with a duette cap/cap and snare, or en bloc resection using an endoscopic knife, and ablative techniques such as radiofrequency ablation (RFA), cryotherapy and argon plasma coagulation. These techniques are complementary and it is increasingly becoming accepted that multimodality therapy results in the best outcome.

There is a growing body of data suggesting that EMR for HGD in Barrett's results in an excellent outcome [3,4]. When used as single modality therapy, it does however result in high recurrence rates of up to 36.7% [5]. This can be reduced to 3% if residual Barrett's is ablated after all visible neoplasia is resected [6]. EMR is essential for all visible lesions and should be considered the ideal treatment for flat neoplasia made visible with advanced imaging techniques. It is our contention that careful assessment with advanced imaging is essential. Usually, when a lesion is visible on white light then the true extent of the lesion is best seen with advanced imaging technique and is generally bigger than what is obvious on white light. It is mandatory to mark the margins of the lesion using advanced imaging technique before ER. The band ligation and cap and snare techniques are both equally effective [7] and either could be used depending on the endoscopist's experience.

Ablative techniques can be used as monotherapy for completely flat and invisible neoplasia. However, attention should be paid to the UK RFA experience. This was not a study purely of RFA and did permit EMR. Early publication suggested a high rate of progression to cancer (3% at 12 months

EXPERT REVIEWS

KEYWORDS: ablation • Barrett's • dysplasia • endoscopic mucosal resection • endoscopic submucosal dissection • intra-mucosal cancer • neoplasia • radiofrequency ablation • submucosal cancer

 10.1586/17474124.2015.1034691 ISSN 1747-4124

increasing to 5.1% at 19 months) [8]. A subsequent follow-up publication on the same series suggested that over time the amount of EMR performed pre-RFA increased from 48 to 60% of cases, with a fall in the need for rescue EMR from 13 to 2% [9]. It is reasonable to hypothesize that this was a result of better case selection with increased recognition of visible lesions over time and more ER prior to RFA. RFA does not result in a tissue specimen so it is important that all visible lesions are resected and sent for histology for proper staging prior to RFA.

It is increasingly recognized that true low-grade dysplasia (LGD) is associated with a significant risk of progression to cancer. RFA as a monotherapy can be effective in these cases, where visible nodules are uncommon and complete eradication of Barrett's can be achieved. The situation in metaplastic Barrett's, however, is quite different. Given the low risk of malignant progression in this cohort, it is our contention that it is unlikely to represent a cost-effective option at this stage. Furthermore, without long-term follow-up data it would be difficult to be certain that ongoing surveillance was unnecessary. Therefore, patients would still need endoscopic surveillance negating many of the benefits of ablation in this group.

Endoscopic therapy is also effective for intra-mucosal cancer. A large series of 1000 cases from Germany has demonstrated cure rates comparable with esophagectomy with no patients dying from advanced cancer in the series [10]. Likewise, providing invasion does not extend beyond the upper third of the submucosa (Sm1), the risk of lymph node metastasis is very low (6%) [11] and some centers are not considering these patients for surgery. The available literature is limited and pathologists find it difficult to distinguish between superficial and deep submucosal invasion, especially on piecemeal resection specimen so careful consideration should be given to the management of these patients.

There has been much controversy around the role of endoscopic submucosal dissection (ESD) in the treatment of Barrett's neoplasia. ESD carries the advantage of yielding an en bloc specimen where invasion depth and lateral margins can be assessed more accurately. However, such techniques are technically challenging and are associated with higher complication rates, including perforation. Furthermore, with excellent results achievable using EMR/RFA combination therapy it has been questioned whether the clinical gains are significant.

It is our contention, however, that ESD does have an important role in the treatment of Barrett's neoplasia. The literature suggests that nodular lesions in Barrett's are highly likely to be cancerous rather then dysplastic. We believe that if the lesion is larger than 20 mm then it is not possible to resect it en bloc using standard EMR technique and should be resected by ESD. A couple of studies [12,13] have proven the safety, efficacy and feasibility of ESD for Barrett's neoplasia in western hands. ESD outcomes will purely depend on the skills and experience of the endoscopist. The ESD learning curve is long and steep in stomach and colon but we believe that ESD in the esophagus is less challenging than in the colon and it is not impossible for western endoscopists to master this technique. In the coming decade, ESD technique is likely to evolve and become easier, faster and safer. As the endoscopist's expertise and skills continue to rise, we are likely to see lot more ESD in the coming decade. It is very important to note that an inexperienced endoscopist performing ESD in the esophagus can do a lot of harm so we call for strict training standards and careful monitoring of outcome if ESD is used in the esophagus.

It is only by having endoscopists who are able to offer the full range of endosocopic therapies (EMR, ESD and ablative techniques) that we will move to making decisions based on pathology rather than availability of skills. This will be the biggest challenge to be faced over the next decade.

Summary

Endoscopic therapy has replaced conventional surgery as the gold standard of care for patients with dysplasia or early mucosal cancer within Barrett's. It has become clear that ER of all visible neoplasia followed by ablation of residual metaplastic Barrett's results in the best long-term outcome. Ablation can be used as a monotherapy for patients with LGD or completely flat HGD, although the number of cases of the latter will be low and ER of all visible neoplasia should be considered as the best approach to treatment.

While the last decade has seen the transition from surgical to endoscopic treatment of Barrett's neoplasia, we believe that the next decade will see the refinement of these endoscopic techniques. ESD will become more common for selected lesions like early SM invasive cancer where surgery is contraindicated. This will require development of good training facilities and refinement of the technique to make it easier and safer. Choices for ablation techniques will increase and the current techniques will evolve to become quicker and more effective.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending or royalties.

No writing assistance was utilized in the production of this manuscript.

References

1. ASGE Standards of Practice Committee. Evans JA, Early DS, et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc 2012;76(6):1087-94
2. Fitzgerald RC, Pietro M, Ragunath K, et al. British society of gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut 2014;63(1):7-42
3. Alvarez Herrero L, Pouw RE, van Vilsteren FG, et al. Safety and efficacy of multiband mucosectomy in 1060 resections in Barrett's esophagus. Endoscopy 2011;43(3):177-83
4. Konda VJ, Gonzalez Haba Ruiz M, Koons A, et al. Complete endoscopic mucosal resection is effective and durable treatment for Barrett's-associated neoplasia. Clin Gastroenterol Hepatol 2014;12(12): 2002-10
5. Pech O, Behrens A, May A, et al. Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. Gut 2008;57(9):1200-6
6. Manner H, Rabenstein T, Pech O, et al. Ablation of residual Barrett's epithelium after endoscopic resection: a randomized long-term follow-up study of argon plasma coagulation vs. surveillance (APE study). Endoscopy 2014;46(1):6-12
7. May A, Gossner L, Behrens A, et al. A prospective randomized trial of two different endoscopic resection techniques for early stage cancer of the esophagus. Gastrointest Endosc 2003;58(2):167-75
8. Haidry RJ, Dunn JM, Butt MA, et al. Radiofrequency ablation and endoscopic mucosal resection for dysplastic Barrett's esophagus and early esophageal adenocarcinoma: outcomes of the UK National Halo RFA Registry. Gastroenterology 2013;145(1):87-95
9. Haidry RJ, Butt MA, Dunn JM, et al. Improvement over time in outcomes for patients undergoing endoscopic therapy for Barrett's oesophagus-related neoplasia: 6-year experience from the first 500 patients treated in the UK patient registry. Gut 2014. [Epub ahead of print]
10. Pech O, May A, Manner H, et al. Long-term efficacy and safety of endoscopic resection for patients with mucosal adenocarcinoma of the esophagus. Gastroenterology 2014;146(3):652-60
11. Gockel L, Sqourakis G, Lyros O, et al. Risk of lymph node metastasis in submucosal esophageal cancer: a review of surgically resected patients. Expert Rev Gastroenterol Hepatol 2011;5(3):371-84
12. Probst A, Aust D, Märkl B, et al. Early esophageal cancer in Europe: endoscopic treatment by endoscopic submucosal dissection. Endoscopy 2015;47(2):113-21
13. Neuhaus H, Terheggen G, Rutz EM, et al. Endoscopic submucosal dissection plus radiofrequency ablation of neoplastic Barrett's esophagus. Endoscopy 2012; 44(12):1105-13