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Management of high grade dysplasia in Barrett's oesophagus with underlying oesophageal varices: A retrospective study

William C. Palmer[a,*], Milena Di Leo[b], Manol Jovani[c], Michael G. Heckman[d], Nancy N. Diehl[d], Prasad G. Iyer[e], Herbert C. Wolfsen[a], Michael B. Wallace[a]

[a] Department of Gastroenterology and Hepatology, Mayo Clinic Jacksonville, USA
[b] Division of Gastroenterology and Gastrointestinal Endoscopy, Vita-Salute San Raffaele University, Scientific Institute San Raffaele, Milan, Italy
[c] Digestive Endoscopy Unit, Division of Gastroenterology, Humanitas Research Hospital, Milan, Italy
[d] Division of Biomedical Statistics and Informatics, Mayo Clinic Jacksonville, USA
[e] Department of Gastroenterology and Hepatology, Mayo Clinic Rochester, USA

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ABSTRACT

Background: Endoscopic treatment of Barrett's oesophagus leading to high grade dysplasia with oesophageal varices may lead to bleeding complications.
Aims: Estimate effectiveness of endoscopic band-ligation in oesophageal varices patients treated for high grade dysplasia, and compare to endoscopically treated non-oesophageal varices high grade dysplasia patients.
Methods: Retrospective comparative study. All 8 high grade dysplasia patients with varices who were treated initially with band-ligation at Mayo Clinic between 8/1/1999 and 2/28/2014 were compared with reference group of 52 high grade dysplasia patients treated endoscopically.
Results: One high grade dysplasia patients patient with oesophageal varices (12.5%) achieved complete remission of intestinal metaplasia defined by at least one followup endoscopy with normal biopsies, and 3 (37.5%) achieved complete remission of dysplasia defined by at least one followup endoscopy with non-dysplastic biopsies. 39 (75.0%) endomucosal resection/radiofrequency ablation patients experienced at least one followup endoscopy with normal biopsies, and 49 (94.2%) experienced non-dysplastic biopsies. Both of these endpoints occurred significantly more often in the endomucosal resection/radiofrequency ablation group compared to the high grade dysplasia with oesophageal varices group ($p = 0.016$ and $p = 0.025$, respectively).
Conclusions: High grade dysplastic Barrett's can be safely managed with band-ligation. However, resolution of Barrett's epithelium is rarely achieved with banding alone.

1. Introduction

Barrett's oesophagus (BE) is directly associated with development of both low grade dysplasia and high grade dysplasia, which can commonly progress to oesophageal adenocarcinoma [1]. Oesophageal adenocarcinoma carries a poor long-term survival outcome, making early treatment of high grade dysplastic Barrett's oesophagus (HGD-BE) indicated even in most high risk groups. The availability of endoscopic therapy for dysplastic BE such as radiofrequency ablation and endomucosal resection, have widely replaced surgical treatment. Cirrhotic patients with portal hypertension leading to oesophageal varices present a unique and challenging cohort of dysplastic BE patients, primarily because of concerns for intra- and post-procedure haemostasis which may limit physician comfort with employing resection or ablation [2–4].

HGD-BE on or adjacent to oesophageal varices warrants intervention, yet little is known regarding either the efficacy or safety of standard BE therapies in this population. Cirrhotic patients with compensated disease or those considered for liver transplantation should have high risk BE addressed. Endoscopic band ligation (EBL) without mucosectomy may be an alternative treatment modality for non-dysplastic BE in selected cases [5]. Data on HGD-BE in cirrhosis is limited to small case series with minimal long term follow up [6]. Outcome and complication rates of HGD-BE patients with oesophageal varices have not been directly compared to non-oesophageal varices patients with HGD-BE.

* Corresponding author at: Mayo Clinic Jacksonville, 4500 San Pablo Road South, Jacksonville, FL 32224, USA. Tel.: +1 9049532000.
E-mail address: Palmer.william@Mayo.edu (W.C. Palmer).

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We have retrospectively evaluated outcomes of endoscopic management of eight cirrhotic patients with oesophageal varices and HGD-BE treated initially with EBL, and compared these cases to a control database of HGD-BE patients treated with endomucosal resection followed by radiofrequency ablation (EMR-RFA). We aimed to describe the outcomes including rates of oesophageal varices resolution, and compare rates of complete resolution of intestinal metaplasia (CRIM), complete resolution of dysplasia (CRD), as well as complications to the control database.

2. Materials and methods

2.1. Patients and data collection

Study subjects were identified by searching the internal ProVation (Wolters Kluwer, USA) endoscopy documentation database for common patients carrying the diagnosis of "oesophageal varices" and "Barrett's oesophagus" at Mayo Clinic in Jacksonville, FL (MCF), Scottsdale, AZ (MCA), and Rochester, MN (MCR). Several additional patients were selected from previous research databases held under Internal Review Board approval by the authors. Fifty clinical charts of patients who had both oesophageal varices and BE were retrospectively reviewed. From these fifty cases, study subjects were excluded if: they did not have pathology consistent with HGD-BE, and/or they were not managed endoscopically with EBL. From these, 8 HGD-BE patients with oesophageal varices were found to have been treated initially with EBL at MCF ($N=6$) or MCR ($N=2$) between August, 1999 and February, 2014. No patients from MCA met the inclusion criteria. In these 8 patients, 34 (4.25 procedures/patient) therapeutic endoscopic procedures were performed and were included in this retrospective study. Additionally, as a comparison group we included all 52 HGD-BE patients without oesophageal varices who were treated with endomucosal resection followed by radiofrequency ablation between September, 2006 and September, 2012 at the MCF. For simplicity, we will refer to these patients as the oesophageal varices banding group and control EMR-RFA group, respectively. Patients were excluded from the control EMR-RFA group if they had undergone endomucosal resection alone, radiofrequency ablation alone, previous treatments for BE or oesophageal adenocarcinoma at an outside institution, if they did not have any follow-up following the start of treatment, or if they had a first radiofrequency ablation that occurred more than 365 days following the first endomucosal resection.

Information was collected on all patients in both groups regarding age, gender, race, Prague C and M class [7], body mass index (BMI), history of smoking, history of chest radiation, history of diabetes, history of oesophagectomy, history of oesophageal cancer, previous aspirin use, previous clopidogrel use, previous Coumadin use, previous proton pump inhibitor (PPI) use, previous statin use, previous non-steroidal anti-inflammatory drug (NSAID) use, hiatal hernia, bleeding, and biopsy findings after the baseline time point. Exclusion criteria included: age less than 18 years, BE without biopsy-proven high grade dysplasia, cause of portal hypertension other than cirrhosis, and those without sufficient follow-up in a surveillance protocol to record post-procedure complications. Patients not found to have high grade dysplasia on biopsy were managed as per Fig. 1, but were not included in this analysis. The baseline date in all analysis was considered to be the date of the first banding procedure in the oesophageal varices patients and the date of the first endomucosal resection in the control EMR-RFA patients. Variceal resolution was defined as the absence of oesophageal varices on a subsequent endoscopy after EBL. CRIM was defined as the occurrence of 2 consecutive normal biopsies after baseline, and CRD was defined as the occurrence of 2 consecutive biopsies of either normal, Barrett's, or indefinite for dysplasia after baseline (i.e. 2 consecutive non-dysplastic biopsies after baseline). Five patients in the oesophageal varices banding group did not have two biopsies performed following the initial banding procedure, and therefore only the remaining 3 oesophageal varices banding patients were included in analysis of CRIM and CRD. All 52 patients in the control EMR-RFA group had sufficient follow-up for CRIM and CRD.

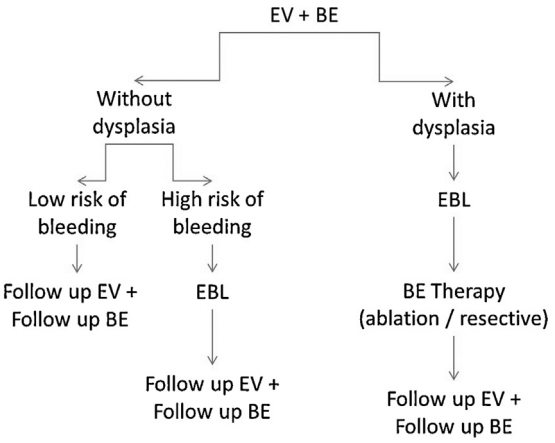

Fig. 1. Flow chart of the protocol management of patients with Barrett's oesophagus and oesophageal varices. Abbreviations: BE, Barrett's oesophagus; EV, oesophageal varices; EBL, endoscopic band ligation.

Although traditionally-defined CRIM and CRD would be ideal endpoints, due to the lack of oesophageal varices banding patients who had sufficient data available for CRIM and CRD assessment, we focused on two less stringent endpoints which all oesophageal varices banding patients had enough follow-up (i.e. at least endoscopy with biopsy following baseline) to assess. These two endpoints are occurrence of a normal set of biopsies from subsequent endoscopy after baseline, and occurrence of a non-dysplastic set of biopsies during subsequent endoscopy after baseline, and in our primary analysis these endpoints were estimated and compared with the reference EMR-RFA patient group. We did also estimate CRIM and CRD in the two patient groups, however no formal statistical comparisons were made due to the very small number of oesophageal varices banding patients for whom this data was available.

In the oesophageal varices banding patient group only, information was also collected regarding liver disease aetiology, history of variceal bleeding, and oesophageal varices resolution. Histological results of biopsy specimens taken from the apex of the band-entrapped pseudopolyp were reviewed. Patients with BE and oesophageal varices were treated according to histological findings (Fig. 1). All patients with BE related dysplasia, irrespective of their risk of bleeding from varices, underwent sequential EBL to achieve oesophageal varices eradication. If BE was still present after variceal resolution, patients were considered for ablative/resective techniques.

2.2. Endoscopic techniques and follow up

In all patients, a complete upper GI endoscopy was performed using a high-definition video endoscope (Olympus, Melville, NY, USA) using standard techniques. Prior to the first treatment, patients with unclear anatomy underwent EUS with a radial echo-endoscope (Olympus, Melville, NY), in order to confirm the presence of Doppler positive oesophageal varices, evaluate oesophageal mucosa and/or nodular lesions, and detect eventual lymphadenopathies [8].