Evolution of the Diagnosis and Management of Barrett's Esophagus: 2004-2014

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Barrett's esophagus (BE) is diagnosed endoscopically when the squamous epithelium, chronically damaged by acid, is transdifferenciated into metaplastic columnar mucosa (1). Often, but not always, the metaplastic columnar epithelia resemble intestinal metaplasia with goblet cells as a key histological marker. Intestinal metaplasia in the esophagus should not be confused with metaplasia of the cardia, which is not uncommon.

Diagnosis of Barrett's esophagus is essentially endoscopic. In order to get a reliable diagnosis of BE, it is important to identify and to properly localize the esophogastric junction (EGJ). There are three relevant anatomical markers that help identify the EGJ: the proximal end of the gastric folds in the cardia, a slight narrowing of the distal esophagus at the top of lower esophageal sphincter, known as the pincers or esophageal press, and the presence of palisade vessels in the distal esophagus. In a normal situation the EGJ and the junction between the squamous mucosa and the columnar mucosal are located halfway between the sphincter complex or high-pressure zone, made of smooth muscle of the lower esophageal sphincter, and the striated muscle of the crura of the diaphragm. Normally, one sphincter is above the other. In the case of hiatal hernia, the internal sphincter moves proximally with respect to the external sphincter (crura of the diaphragm). A mild separation of both sphincters can only be detected with high resolution manometry. A hiatal hernia is identified by endoscopy when the internal sphincter is demonstrably above the imprint of the crura of the diaphragm in the esophageal hiatus. Unfortunately, endoscopic diagnosis of hiatal hernia is prone to error because of over-insufflation, retching, vomiting and confusion about the vasculature of the cardia (which is often not visible) with palisade vasculature in the distal esophagus. Here are some recommendations for proper diagnosis of hiatal hernia:

1. Evaluate the EG junction while the patient is breathing quietly.
2. Evaluate the EG junction in the absence of vomiting or retching
3. Avoid over-insufflation
4. Avoid angulation while withdrawing the endoscope
5. Look closely at, and measure, the distance between the internal sphincter gastro esophageal junction and upper esophageal sphincter.

Adoption of these recommendations should reduce the number of erroneous diagnoses of hiatal hernia.

Once the EGJ has been clearly identified, the columnar mucosa above this level should be identified as columnar metaplasia or BE. The extension of metaplastic changes must be measured according to the Prague criteria. The C value is the circumferential

extension, and M is the maximum extension of the compromised area. When the values of C and M can be stated with certainty, terms such as long, short or ultra-short BE are not necessary. Documentation of intestinal metaplasia with goblet cells, as required in the American guidelines for BE diagnosis, is not absolutely necessary for various reasons (2). This is especially true for short segments of metaplasia and for neoplastic changes without metaplasia in the nearby intestinal tissue (3).

The importance of recognizing BE is related to the associated risk of developing cancer, although this risk is actually less than had once been thought (4). The current low risk is largely explained by the extensive use of PPIs (proton pump inhibitors) (5). It seems that in these cases neoplasia develops from non-dysplastic mucosa to low and high grade dysplasia to invasive carcinoma. Low-grade dysplasia is over-diagnosed in daily practice due to confusion between inflammatory and reactive changes that can suggest malignancy. To rule out neoplasia, biopsies should be obtained after sustained acid suppression therapy to decrease inflammation induced by GERD. Ideally, these biopsies should be evaluated by pathologists who are experts in the gastrointestinal tract. Preferably, high-resolution endoscopes should be used to evaluate the mucosa. The mandatory use of narrow band imaging or related techniques is controversial, although these techniques are used in referral units (6).

Neoplastic changes may occur as a visible focal alterations of the mucosa and must be graded according to the Paris classification. Early neoplasms are most frequently found in positions between 2 and 5 o'clock (7). It is not uncommon that neoplasia is not detectable by endoscopy. Random biopsies of the four-quadrants at intervals of one to two inches in the BE segment are recommended for detecting hidden neoplasms. When a lesion is detected, estimation of the depth of invasion by endoscopic ultrasound is not necessary in order to proceed to endoscopic intervention (8).

Any focal abnormality should be endoscopically resected using rubber band ligation or endoscopic dissection. An expert and focused assessment of the resected specimen will allow an adequate estimate of the depth of infiltration in case of invasive tumor growth. The normal mucosa adjacent to the lesion should be fully eradicated with circumferential or partial radiofrequency ablation (RFA). Acid suppression should be continued to allow healing of the squamous mucosa and may help to prevent recurrence of the columnar metaplasia. The long-term results appear to be rewarding (9, 10).

Before performing RFA of BE with high or low grade dysplasia, different scenarios that might result in better outcomes should be considered:

1. Only patients with well documented low grade dysplasia should be treated with RFA, and only when two pathologists concur. Only 15% of the patients who are initially diagnosed with low grade dysplasia (LGD) have those diagnoses confirmed in centers with expert pathologists (11-13). Furthermore, even when LGD is confirmed by expert pathologists, a large percentage (28%) suffer relapses over time as shown by Phoa (14). In that study, histological confirmation was the most important selection criteria for therapy on only one occasion. Nevertheless, selection of patients diagnosed with LGD after several endoscopies refines the process of selecting patients with dysplasia and a risk of progression. In addition, the possibility of progression from LGD to HGD makes the RFA procedure worthwhile to consider.
2. Better methods are needed to determine the risks of progression in patients with BE whether or not they have dysplasia. The multivariate analysis in another article by Phoa determines that circumferential BE, time after diagnosis of BE, and time after the diagnosis of dysplasia are predictors of progression (15). However, biological, molecular and histological markers are clinical and research priorities for identifying candidates for ablation and/or resection (16-18).
3. Radio frequency ablation does not completely eliminate the risk of persistence or progression of BE. A quarter of the patients in various studies have require additional endoscopic treatment to complete tissue removal (19). However, these new interventions do not diminish the value of RFA but reflect the complex and unique nature of the anatomical and biological behavior of BE.
4. Follow-up for these patients is marked by the possibility of recurrence and there are no well-established protocols for follow-up, endoscopic technique and timing for these patients (20). Both patients and physicians must have a high commitment when embarking on proactive management of BE with dysplasia. A higher number of interventions are associated with a lower quality of life because of the adverse effects of ablation and resection. However, there are inherent psychological implications for patients living with a disease that has a rapid rate of progression.
5. None of the recent studies of RFA in for treatment of dysplastic BE assess the great clinical impacts of the therapy in the same way that they assess the impacts of cancer and death due to cancer even though there are important ethical implications. Esophageal cancer metastasizes quickly, has high rates of perioperative morbidity and mortality, and the five year survival rate is less than 20%.

6. Medical centers with expertise in these treatments produce results that are not widely reproducible in the patient population of general medical practice.
7. En el presente número se muestra la evolución en el enfoque y manejo de los pacientes con EB asociado a displasia o el carcinoma in situ, inicialmente la terapia se centró en la ablación con argón plasma con resultados poco alentadores por la alta recurrencia asociada a los EB más largos. Se implementó la práctica de la mucosectomía con bandas y se complementaba con argón plasma con resultados más alentadores y en la actualidad la terapia se hace en el compromiso circunferencial con RFA y en los casos de nodulaciones con la mucosectomía con bandas seguida por RFA. Los diferentes estudios proveen importante evidencia para apoyar el uso de la ablación por radiofrecuencia no sólo en pacientes con displasia de alto grado y el cáncer temprano, también para la displasia de bajo grado confirmada y en los pacientes seleccionados con EB. Un enfoque proactivo endoscópico para eliminar la displasia puede resultar en la reducción de la morbilidad y la mortalidad relacionadas con la progresión de esta enfermedad.

This issue of the Review shows the evolution that has occurred in the approach and management of patients with BE associated with dysplasia or carcinoma in situ. Initially, therapy focused on argon plasma ablation with results that were not very encouraging because of the high rates of recurrence with longer BE. The band mucosectomy technique was implemented and complemented with argon plasma with more encouraging results. Nowadays this technique is performed when there is circumferential compromise with RFA. In the cases of nodules, band mucosectomy is followed by RFA. Various studies provide important evidence to support the use of radiofrequency ablation not only in patients with high-grade dysplasia and early cancer, but also in patients with confirmed low-grade dysplasia and in selected patients with BE. A proactive endoscopic approach to eliminating dysplasia can result in reducing the rates of morbidity and mortality associated with the progression of this illness.

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