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Original Article

Management of Barrett's Esophagus

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Abstract **Barrett's esophagus is a precancerous abnormality commonly associated with chronic gastroesophageal reflux disease (GERD). In this update we briefly review the pathogenesis, risk factors, screening, monitoring and treatment of the disease. We emphasize the need for early detection and management of Barrett's esophagus with high grade dysplasia. Both endoscopic and surgical options for treatment are highlighted. A summary of the results of treatment from the literature is presented. This review should be useful for busy general surgeons and residents as a quick refresher on the state-of-the-art knowledge of Barrett's esophagus.**

Keywords: **Barrett's esophagus, GERD, adenocarcinoma**

Barrett's Esophagus (BE) is a pre-cancerous abnormality in which the squamous type epithelium in the lower esophagus is replaced by columnar epithelium with metaplasic changes. BE is most often diagnosed in people who have chronic gastroesophageal reflux disease (GERD). It is estimated that about 10% of patients who have chronic GERD will develop BE. Of these about 10% will go on to develop dysplasia, which then may progress to adenocarcinoma. The highest incidence of BE is found in the western part of the world such as the U.S. and Europe[1,2].

Pathogenesis

GERD is the most important risk factor preceding the occurrence of BE[3,4]. BE patients often have symptoms of severe and chronic acid reflux which may be combined with decreasing lower esophageal sphincter tone. The disease is primarily caused by acid reflux, but can less commonly also result from prolonged bile reflux into the esophagus[5].

Obesity is also associated with the occurrence of BE, there is a higher incidence of GERD in obese people, and GERD causes BE. However, medical science still does not understand clearly why obese people are prone to acid reflux disease[6], although there are several assumptions, such as obesity causes more abdominal fat which causes pressure in the abdomen and pressure in the stomach, which finally causes acid reflux[7]. In addition, obesity is also associated with adenocarcinoma-type cancers of the esophagus[8-10].

A small number of BEs have a congenital cause, although a low proportion compared to other risk factors. Studies have found that about 7% of BE patients have a history of BE in the first or second family hierarchy[11,12]. The congenital BE patients are usually young, and BE in this age group is not associated with

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obesity. This genetic pathogenesis may be an autosomal dominant abnormality[13,14].

Screening

BE screening is important because it offers several advantages such being reliable and cost-efficient, and focusing on the higher-risk population, patients with chronic GERD. It is also effective in that treating the disease is more effective if it is detected early. The population at highest risk recommended for screening is Caucasoid men older than 50 years with symptoms of acid reflux disease, or those recommended by a physician[15].

General screening is based on endoscopy and biopsy of suspected lesions for pathological examination and diagnosis. The main area normally screened is the lower esophagus and the junction between the esophagus and stomach. Overall, this method has a sensitivity of 82% and a positive predictive value 34% in symptomatic Caucasoid patients or others suspected of having BE. The positive predictive value drops to 15% in the case of African men[16]. Males have twice the incidence of BE of females[17]. Endoscopic biopsy for BE generally uses the Seattle protocol (four quadrant biopsies at 1 cm intervals)[18].

Treatment

When a patient has been diagnosed with BE, the normal first-line treatment is recommending conservative life-style modifications such as reducing smoking and weight reduction, with regular medical supervision to follow the course of the disease[19]. A proton pump inhibitor (PPI) is also routinely prescribed as standard treatment for BE. A recent 5-year follow-up U.S. study reported that PPIs can reduce the incidence of dysplasia in patients with BE by up to 75%[20]. Another study from Australia, with a median follow-up of 4.5 years, found that patients who did not take a PPI had a risk of low grade dysplasia 5.6 times greater than patients who did take a PPI, and a risk of high grade dysplasia or cancer 20.9 times greater than the PPI group[21].

In addition to drug treatment of patients with BE, fundoplication is often recommended, with a surgical endoscopic approach through the abdomen (laparoscopic fundoplication) to enhance the strength of the lower esophageal sphincter. The hope is that it can reduce acid reflux and decrease the BE, or at least prevent the disease from progressing to dysplasia or esophageal cancer[22]. However, a meta-analysis comparing PPI groups with anti-reflux surgery groups to prevent BE found that the incidence of cancer patients per year was 4.8/1000 in surgical group and 6.5/1000 in the drug group, which was not statistically significantly different ($p = 0.32$)[22]. This result was also noted in other studies[23,24].

Monitoring

The recommendations for monitoring BE patients varies with the level of dysplasia. In general, in the absence of endoscopic esophageal dysplasia, a repeat biopsy is recommended in one year, at which time, if there is still no dysplasia, the recommendation is surveillance with endoscopy and biopsy every 3-5 years. In the case of low grade dysplasia, the recommendation is endoscopy and repeat biopsy in six months and following repeated once a year. In the case of high grade dysplasia, the doctor should consult a pathologist to confirm the finding. For selected cases not treated by esophagectomy or therapeutic endoscopic procedure, it is suggested that a repeat biopsy be done every three months[15,25-27].

High grade dysplasia (HGD) management

The diagnosis of patients with HGD is very important because it is the precursor and marker for the development to adenocarcinoma. Generally BE without dysplasia will progress to cancer in 3.3 to 5.69 cases/1,000/year[28,29]. In cases of low grade dysplasia (LGD) the incidence increases to 16.9 cases/1,000/year[29], and for HGD, the incidence is as high as 65.8/1,000/year[30].

The doctor must always exercise caution in the diagnosis or detection of HGD, even after endoscopic biopsy and be careful to provide regular follow up. It is thus important for the doctor to explain to the patient the importance not missing the follow-up endoscopy appointments[31].

Endoscopic therapy

The two most often used techniques of endoscopic treatment are ablation and resection. The first technique uses heat, chemicals, laser or radiofrequency to destroy the abnormal mucosa of the esophagus. However, these methods cannot harvest tissue for pathological examination since it has been destroyed.

Table 1 The treatment results of esophageal surgery in patients with HGD and early esophageal cancer (modified from Gilbert, et al.[40])

		Pathological stage (n)				Complications (%)		
Study	**n**	HGD	0	1	operation	morbidity	leak	Mortality
Prasad (2007)	70	1	4	5	THE/TTE	38	0	1.4
Williams (2007)	38	28	4	5	THE/TTE	37	3	0
Peyre (2007)	49	20	29	-	VES/THE/TTE	35	2	2
Moraca (2006)	36	11	11	12	TTE/THE	44	5.6	0
Reed (2005)	49	31	-	9	THE/TTE	NR	4	2
Rice (2006)	111	59	40	6	NR	NR	NR	0
Chang (2005)	34	14	9	7	THE/TTE	29	3	0
Westerterp (2005)	120	13	41	76	THE	NR	NR	4

THE = transhiatal esophagectomy
TTE = transthoracic esophagectomy
VSE = vagal nerve sparing esophagectomy
NR = not reported

The other common technique is resection, which involved cutting out the abnormal mucosa of the esophagus. This technique has the advantage of retaining post-procedure abnormal tissue for pathological examination, which can detect abnormal spread of cancer cells if present, and affect the decision on further treatment. However, this method relies on the expertise of the doctor, as it is a delicate procedure which can have severe complications such as esophageal perforation or long-term postoperative esophageal stricture[32].

Treatment with surgery

Patients diagnosed with HGD are at high risk to have early stage esophageal cancer, because small biopsies taken from a random site can easily miss areas of abnormal mucosa. A study in 111 BE patients who had been diagnosed with HGD on biopsy from esophagoscopy and treated with an esophagectomy found that 45% had early stage esophageal cancer[33]. A number of studies have found that HGD patients had a 14-59% chance to progress to esophageal cancer[34,35]. Doctors who support an esophagectomy for HGD give the reason that if HGD progresses to early esophageal cancer, the cancer is likely to spread to nearby lymph nodes which makes the prognosis worse[36,37]. An esophagectomy can remove both the esophagus and peri-esophageal lymph nodes. The surgical procedure can use either a transthoracic or transhiatal approach, and either technique can use an open surgical incision (open surgery) or thoraco-laparoscopy (minimal invasive surgery) approach. Minimally invasive surgery helps in reducing some complications after surgery such as postoperative pain, and helps the patient recover faster[38].

Results of surgical treatment

Table 1 is a summary of the results of a number of studies involving patients with HGD and early esophageal cancer who were treated with surgery to remove the esophagus. In HGD patients there will be no chance of esophageal cancer later, in contrast to patients with early esophageal cancer who are likely to have a cancer recurrence after surgery. In particular, one study found that the group in which the cancer had spread to the lymph nodes had a 5-year recurrence free survival of only 33% compared with the group in which the cancer had not spread to the lymph nodes, which had a 94% recurrence-free rate[39]. Similarly, the 5-year survival rate after surgery in HGD patients was 95%, while the cancer patient group was only 64%.

However, the esophagectomy procedure is a major surgery, with a chance of complications of about 33% and an anastomosis leakage rate of 2.8%, while the likelihood that the patient will die from the surgery is 1.4%[40]. The most important factor for good postoperative results is treatment at a hospital with a high volume of esophageal surgery with expert surgeons[33].

Conclusion

Patients with chronic GERD should have a BE screening test, as this disorder has a high risk of progressing to cancer of the esophagus. If BE is detected, it must be treated by treating the GERD. A

follow-up endoscopy is highly recommended. BE patients with HGD should be treated as special cases because there is a risk of early stage esophageal cancer. Treatment options include esophageal endoscopic treatment and surgery to remove the esophagus, depending on the opinion of the treating doctor and wishes of the patient.

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