

INTRODUCTION

Esophageal cancer is the seventh leading cause of all deaths from cancer worldwide, with an estimated 14,000 deaths from this cancer in the United States alone in 2006 (*Parakrama et al., 2006*).

Special attention is being paid to Barrett's esophagus (BE) as it has been recognized as a precursor for esophageal adenocarcinoma (EAC) (*Pohl and Welch, 2005*).

Random four quadrant biopsies are the standard method used for detection of dysplasia in Barrett's esophagus but it is commonly known that apart from being time consuming and uncomfortable random biopsies are associated with sizeable sampling errors (*Mandal et al., 2003*).

Magnifying chromoendoscopy has been used in the evaluation of GERD and Barrett's esophagus. GERD was associated increased vascularity at SCJ (squamo-columnar junction) and specific mucosal pattern has been correlated with histopathological findings and found to be useful in evaluation of BE (*Sharma et al., 2003*).

Narrow-band imaging (NBI) is a relatively new high-resolution endoscopic technology that helps identify potentially neoplastic changes of the gastrointestinal epithelium. Its use is rooted in the concept that the depth of light penetration depends upon its wavelength. As opposed to conventional white-light

endoscopy (WLE), NBI utilizes 2 distinct wavelengths of light, 415 nm(blue) and 540 nm (green), with bandwidths of 20–30 nm each, limiting penetrance of the light to the mucosal surface (*McKinley et al., 2008*).

The blue light highlights the superficial capillary networks, whereas the green light focuses on the subepithelial vessel (*Wolfsen et al., 2008*).

A number of reports have indicated that NBI may also be helpful in revealing suspicious areas in BE (*Sharma et al., 2006*). In this regard, it has been postulated that NBI may lead to the same contrast enhancement capabilities as chromoendoscopy but without its disadvantages (*Curvers et al., 2007*).

AIM OF THE WORK

The aim of this study was to evaluate the role of High resolution magnification endoscopy with Narrow band imaging in improving the endoscopic diagnosis of Barrett's esophagus.

GROSS ANATOMY OF THE ESOPHAGUS

The esophagus is a flattened muscular tube of 18 to 26 cm from the upper sphincter to the lower sphincter. It connects the pharynx to the stomach. Beginning in the neck, at the pharyngoesophageal junction (C5-6 vertebral interspace at the inferior border of the cricoid cartilage), the esophagus descends anteriorly to the vertebral column through the superior and posterior mediastinum. After traversing the diaphragm at the diaphragmatic hiatus (T10 vertebral level) the esophagus extends through the gastroesophageal junction to end at the orifice of the cardia of the stomach (T11 vertebral level) (*Long et al., 2002*).

Topographically, there are three distinct regions: cervical, thoracic, and abdominal.

- The cervical esophagus extends from the pharyngoesophageal junction to the suprasternal notch and is about 4 to 5 cm long.
- The thoracic esophagus extends from the suprasternal notch to the diaphragmatic hiatus, passing posterior to the trachea, the tracheal bifurcation, and the left main stem bronchus.
- The abdominal esophagus extends from the diaphragmatic hiatus to the orifice of the cardia of the stomach. Forming a

truncated cone, about 1 cm long, the base of the esophagus transitions smoothly into the cardiac orifice of the stomach.

- Two high-pressure zones prevent the backflow of food: the upper and lower esophageal sphincter (**Kumar et al., 1989**).

Blood Supply

The rich arterial supply of the esophagus is segmental.

- The branches of the inferior thyroid artery provide arterial blood supply to the upper esophageal sphincter and cervical esophagus.
- The paired aortic esophageal arteries or terminal branches of bronchial arteries supply the thoracic esophagus.
- The left gastric artery and a branch of the left phrenic artery supply the LES and the most distal segment of the esophagus (**Kumar et al., 1989**).

The venous supply is also segmental. From the dense submucosal plexus the venous blood drains into the superior vena cava. The veins of the proximal and distal esophagus drain into the azygous system. Collaterals of the left gastric vein, a branch of the portal vein, receive venous drainage from the mid-esophagus. The submucosal connections between the portal and systemic venous systems in the distal esophagus form esophageal varices in portal hypertension. These submucosal varices are sources of

major GI hemorrhage in conditions such as cirrhosis (*Kumar et al., 1989*).

Innervation

The esophagus, like the rest of the viscera, receives dual sensory innervation, traditionally referred to as parasympathetic and sympathetic, but more properly based on the actual nerves, vagal, and spinal (*Goyal et al., 1999*). The motor innervation of the esophagus is predominantly via the vagus nerve. The esophagus receives parasympathetic and sympathetic innervation that regulates glandular secretion, blood vessel caliber, and the activity of striated and smooth muscle (*Kumar et al., 1989*).

Lymphatics

Lymphatic drainage in the esophagus consists of two systems: the lymph channels and lymph nodules. The lymph channels begin in the esophageal tissue space as a network of endothelial channels (20–30 μm) or as blind endothelial sacculations (40–60 μm). Lymph capillaries drain into collecting lymph channels (100–200 μm). Paired semilunar valves within the collecting channels determine the direction of flow. The collecting lymph channels merge into small trunks that open into the regional lymph nodes. As with esophageal innervation, the lymphatic drainage of the esophagus differs in the striated and smooth muscle regions. The lymphatics from the proximal third of the esophagus drain into the deep cervical lymph nodes, and subsequently into the thoracic duct. The lymphatics from

the middle third of esophagus drain into the superior and posterior mediastinal nodes. Lymphatics of the distal third of the esophageal follow the left gastric artery to the gastric and celiac lymph nodes (*Long et al., 2002*).

Musculature of the Esophagus

The muscular coat consists of an external layer of longitudinal fibers and an internal layer of circular fibers. The longitudinal fibers descend in the esophagus and combine to form a uniform layer that covers the outer surface of the esophagus. The circular muscle layer provides the sequential peristaltic contraction that propels food toward the stomach. The circular fibers are continuous with the inferior constrictor muscle of the hypopharynx; the internal muscular layer is thicker than the external muscular layer. Below the diaphragm, the internal circular muscle layer thickens and the fibers become semicircular and interconnected, constituting the intrinsic component of the lower esophageal sphincter (LES) (*Sivarao et al., 2000*).

Upper Esophageal Sphincter

The upper esophageal sphincter (UES) is a high-pressure zone situated between the pharynx and the cervical esophagus. It is a musculo-cartilaginous structure composed of the posterior surface of the thyroid and cricoid cartilage, the hyoid bone, and three muscles: cricopharyngeus, thyropharyngeus, and cranial cervical esophagus. Each muscle plays a different

role in upper esophageal sphincter (UES) function (*Sivarao et al., 2000*).

Upper esophageal sphincter function is controlled by a variety of reflexes that involve afferent inputs to the motor neurons innervating the sphincter. The cell bodies of the vagal efferent fibers innervating the upper esophageal sphincter and the proximal striated muscle esophagus arise in the nucleus ambiguus. These reflexes elicit either contraction or relaxation of the tonic activity of the UES. Inability of the sphincter to open or discoordination of timing between the opening of the UES with the pharyngeal push of ingested contents leads to difficulty in swallowing known as oropharyngeal dysphagia (*Sivarao et al., 2000*).

Lower Esophageal Sphincter

The lower esophageal sphincter is a high-pressure zone located where the esophagus merges with the stomach. The LES is a functional unit composed of an intrinsic and an extrinsic component. The intrinsic structure of LES consists of esophageal muscle fibers and is under neurohormonal influence. The extrinsic component consists of the diaphragm muscle, which functions as an adjunctive external sphincter that raises the pressure in the terminal esophagus related to the movements of respiration. Malfunction in any of these two components is the cause of gastroesophageal reflux and its subsequent symptoms and mucosal changes (*Delattre et al., 2000*).

The LES is innervated by both parasympathetic (vagus) and sympathetic (primarily splanchnic) nerves, with the vagal pathways being essential for reflex relaxation of LES. Vagal sensory afferents from the LES and distal esophagus end in nucleus tractus solitarius of the hindbrain. The motor innervation of the LES is topographically provided through preganglionic fibers from the dorsal motor nucleus of the vagus. The dorsal motor nucleus and the tractus solitarius nucleus form a dorsal vagal complex in the hindbrain that coordinates reflex control of the sphincter (*Hornby et al., 2000*).

An Endoscopic View of the Normal Anatomy around the Gastroesophageal Junction

Distal Esophagus and Lower Esophageal Constriction

The lower esophageal constriction is formed by a combination of the lower esophageal sphincter and extrinsic pressure from the diaphragmatic hiatus. It is reached at approximately 36–38 cm from the incisor teeth. The lumen of the distal esophagus appears round and symmetrical. The muscular contraction and accompanying venous plexus create a typical endoscopic picture of longitudinal folds with concentric luminal narrowing (*Block et al., 2004*).

Gastroesophageal Junction

The gastroesophageal junction is reached at approximately 38(35–41) cm from the incisors. Besides the indentations from the aorta, left main bronchus, and heart, which give the esophagus a somewhat more variegated appearance, the gastroesophageal junction is the first truly interesting station that is reached during upper endoscopy. At the same time, this region is one of the most frequent indications for upper GI endoscopy and is the site of the most common diseases of the esophagus and of the upper gastrointestinal tract in general. Endoscopy is excellent for evaluating the morphology of this region. The endoscopist identifies and evaluates the sphincter itself, the diaphragmatic hiatus, and the transitional region between the squamous epithelium of the esophagus and the columnar epithelium of the

stomach, which are separated by a visible junction called the Z-line (*Block et al., 2004*).

Lower Esophageal Sphincter and Diaphragmatic Hiatus

The lower esophageal sphincter is an approximately 3-cm-long (2–4 cm) segment in the distal esophagus. It can be identified manometrically by its resting pressure of 15–25mmHg and, less confidently, by its anatomical features. The sphincter zone lies partly above and partly below the diaphragm in the region of the esophageal hiatus. The Z-line in its lower portion marks the boundary between the esophageal squamous epithelium and gastric columnar epithelium (the squamocolumnar junction). Endoscopically, sphincter closure in a healthy subject creates a rosette pattern with the lumen being precisely centered at the point where four to six longitudinal folds in the distal esophagus converge, with viewing from a level just above the sphincter, especially with air insufflation, will reveal peristaltic waves followed by a transient opening of the sphincter segment, briefly exposing the Z-line and the interior of the stomach (*Wallner et al., 2002*).

Following careful inspection of this region, the endoscope is gently advanced at a moment when the sphincter is relaxed. The action of the diaphragm muscles can often be seen as respiration dependent luminal constrictions, especially if the sphincter does not close too tightly. The examiner evaluates the sphincter segment, its distance from the incisor teeth, its functional competence, and the diaphragmatic hiatus.

It is particularly important to assess whether the lower esophageal sphincter is competent or incompetent, although this assessment varies considerably among different examiners. The position of the diaphragmatic hiatus is also assessed in relation to the incisor teeth, the lower esophageal sphincter, and the Z-line (**Block et al., 2004**).

Z-Line

The Z-line, the boundary between the esophageal and gastric epithelium, should be identified, localized, and evaluated in every upper endoscopy. The location of the Z-line is measured in centimeters from the incisor teeth, with a normal range of 36–40 cm. The relation of the line to the esophageal hiatus should also be described. This relation is variable and depends upon respiration, the axial pressure applied with the endoscope, and constitutional factors. The Z-line is located at or slightly above the level of the esophageal hiatus (**Wallner et al., 2002**).

The endoscopic appearance of the Z-line is highly variable. It usually has a jagged or undulating shape and is basically symmetrical (**Block et al., 2004**).

The gastric mucosa appears redder, fresher, and slightly raised in relation to the pale pink or gray epithelium of the esophagus. The boundary line may be very irregular; “flames” of gastric mucosa may project into the esophagus, just as tongues of esophageal epithelium may extend downward. These

extensions may be largely uniform and symmetrical, or they may have a completely asymmetrical aspect. Occasionally the epithelial boundary appears blurred or indistinct, but usually it is sharply defined. The line may show hypertrophic thickening or may even form a functionally active ring (***Block et al., 2004***).

GASTROESOPHAGEAL REFLUX DISEASE

Definition

A current definition of the disorder is “a condition which develops when the reflux of stomach contents causes troublesome symptoms (i.e., at least two heartburn episodes per week) and/or complications.” (*Vakil et al., 2006*).

Gastroesophageal reflux disease is the most common gastrointestinal diagnosis recorded during visits to outpatient clinics (*Shaheen et al., 2006*).

Evidence indicates that up to 36% of otherwise healthy persons suffer from heartburn at least once a month, and that 7% experience uncomplicated GERD and symptoms of heartburn as often as once a day. It has been estimated that approximately 2% of the adult population suffers from complicated GERD, associated with macroscopic or histologic damage to the esophagus. The incidence of GERD increases after the age of 40, and it is not uncommon for patients experiencing symptoms to wait years before seeking medical treatment (*Vakil et al., 2006*).

Risk Factors

Obesity is a major risk factor (*Jacobson et al., 2006*). Symptoms may be aggravated by spicy or fatty foods, caffeine, alcohol, citrus fruits, recumbency or bending forward (*Richter, 2007*).

GERD may also be provoked by certain medications such as calcium channel blockers and may be mimicked by other drugs such as bisphosphonates and non-steroidal anti-inflammatory drugs (NSAIDs) (**Leong et al., 2006**).

Impaired clearance of the refluxed gastric juice from the esophagus also contributes to damage in many patients. Whereas some gastroesophageal reflux is normal, several factors may predispose patients to pathologic reflux, including hiatus hernia (**DeVries et al., 2008**), lower esophageal sphincter hypotension, loss of esophageal peristaltic function, abdominal obesity (**Corley et al., 2007**), increased compliance of the hiatal canal (**Pandolfino et al., 2003**) and gastric hypersecretory states (**Hirschowitz, 2004**).

GERD Syndromes

GERD Syndromes are divided as esophageal and extra esophageal syndromes. The esophageal syndromes include symptomatic syndromes and syndromes with injury (**Vakil et al., 2006**).

Esophageal syndromes

Symptoms (with or without esophageal injury)

Common symptoms: Heartburn, regurgitation, dysphagia, chest pain. Less common symptoms: Odynophagia (pain with swallowing), water brash (excessive salivation prompted by acid reflux), subxiphoid pain, nausea (**Vakil et al., 2006**).