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Advancements in Esophageal Stricture Treatment: The Role of Stents in Benign and Malignant Conditions

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Abstract

The present study aimed to investigate advances in the treatment of esophageal stricture and the role of stents in benign and malignant diseases. The esophagus is a muscular tube that plays a crucial role in the process of swallowing and transports both solids and liquids from the pharynx to the stomach. Its development involves contributions from the embryonic endoderm, mesoderm, and neural crest cells. Esophageal pathology is diverse, and surgical procedures for its correction often require ongoing enhancements. Barrett's esophagus, which is most often caused by gastroesophageal reflux, is a common condition, though strictures may also develop due to neoplastic causes or chemical burns. A thorough understanding of the anatomy and physiology of the esophageal is crucial for both internal medicine and surgical treatment approaches. In recent years, the treatment of esophageal strictures has relied heavily on esophageal stents, which are made of materials such as metal, polymer, or biodegradable substances. While the clinical outcomes are generally favorable, complications are common. The first recorded attempt at stenting dates back to the mid-19th century using an ivory tube. In cases involving the ingestion of caustic substances, both dilation and stenting show promising results. However, these procedures are associated with various complications, ranging from pain to incomplete stent expansion.

Keywords: Esophagus, Esophageal stents, Esophageal strictures, Endoscopic procedure

Introduction

The esophagus is a muscular tube responsible for carrying food from the throat to the stomach. During development, the esophagus originates from the foregut, a region of the embryo that is influenced by various growth factors. These factors, including proteins like Wnt5a, Six2/Sox2, and Hoxa, help guide the migration of neural crest cells. In weeks 7 and 8 of development, the foregut undergoes a process where its lumen becomes almost fully occluded [1].

Around the 10th week, the lumen starts to reopen through a process called vacuolization. This change results in the formation of the esophagus, initially lined with ciliated epithelium. Eventually, the ciliated layer is replaced by squamous epithelium, although small patches of ciliated epithelium remain to form the esophageal glands. The mucosal and submucosal layers of the esophagus originate from the endoderm. The smooth muscle layer and the myenteric plexus begin to form around the sixth week of development, and blood vessels start to develop by the seventh week. The smooth muscle in the lower esophagus comes from the mesoderm surrounding the foregut, while the upper esophagus's striated muscle originates from the mesenchymal arches. The middle esophagus contains both smooth and striated muscles, but

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the specific origins of these muscles are not fully understood. By the ninth week, the smooth muscle differentiates into circular and longitudinal layers. The neural crest cells form the myenteric plexus by the fourth week, migrating to the hindgut by the seventh week. By the sixth week, the neural crest also migrates through the circular muscle layer to form the submucosal plexus. Interstitial cells of Cajal, which are critical for muscle contraction, form after smooth muscle differentiation and do not require neural crest cells for their formation [2, 3]. The present study aimed to investigate advances in the treatment of esophageal stricture and the role of stents in benign and malignant diseases.

Results and Discussion

Normal anatomy of the esophagus

The length of the esophagus typically ranges from 18 to 26 cm. The diameter of the esophagus when food passes through it measures approximately 2 cm in the anteroposterior direction and 3 cm laterally. One of the most common pathologies related to the esophagus is the Bartholian esophagus, which is frequently linked to gastroesophageal reflux disease (GERD) [4, 5].

Topography of the esophagus

The esophagus is divided into three sections: the cervical, thoracic, and abdominal regions. The cervical esophagus extends from the hypopharynx to the thoracic inlet. The upper thoracic esophagus stretches from the thoracic inlet to the lower border of the azygos vein. The middle thoracic esophagus lies between the azygos vein and the inferior pulmonary vein. Finally, the lower thoracic esophagus extends from the inferior pulmonary vein to the stomach [6].

Esophageal pathology

Esophagitis is the most common form of inflammation in the esophagus. It is typically marked by thickened longitudinal folds due to edema and inflammation. In long-term cases of GERD, an esophageal inflammatory polyp may form, typically located at the cardiac orifice. Scarring caused by GERD can be observed through a barium swallow exam, which shows longitudinal folds converging toward the scarred site. Chronic inflammation can lead to the formation of a circular stricture located above a hiatal hernia [7].

Esophageal conditions and functional insights

The esophagus may occasionally develop a ring-shaped formation, which can sometimes be mistaken for the Schatzki ring in individuals suffering from dysphagia. Additionally, esophageal scarring may result in a shortening of the organ's length, causing a step-ladder appearance. This must be carefully distinguished from the fine longitudinal striations associated with a condition known as feline esophagus, commonly linked to acid reflux [7].

Barrett's esophagus arises from a transformation of the normal esophageal lining into tissues that resemble those of the stomach or intestines. This condition affects about 10% of individuals with gastroesophageal reflux disease (GERD). The primary function of the esophageal mucosa is to shield the underlying layers from harmful substances in food and liquids. It contains minor salivary glands that secrete bicarbonate to neutralize stomach acid. Additionally, the mucosal layer features muscularis mucosae, an important structure for distinguishing the mucosa from the surrounding tissues [8, 9].

Microscopic and cellular analysis

In advanced microscopic studies, a variety of cells have been identified in the esophageal lining, including melanocytes, Langerhans cells, Merkel cells, and inflammatory cells like lymphocytes. These cells generally lack desmosomes, with the exception of Merkel cells, which do contain them. Melanocytes, which produce melanin, are found among keratinocytes, while Langerhans cells can migrate to regional lymph nodes and present antigens to T-helper lymphocytes. Merkel cells, which play a crucial role in touch sensation, are connected to surrounding cells through desmosomes. Additionally, inflammatory cells such as polymorphonuclear lymphocytes and mast cells are also present in the tissue [10].

Esophageal function and physiological mechanisms

The upper esophageal sphincter is a high-pressure area located between the larynx and the top portion of the esophagus. It has elastic and tonic characteristics that allow it to expand sufficiently to facilitate food passage. Its main role is to prevent food from entering the airways and to regulate the amount of air entering the digestive tract [11-13].

The sphincter is formed by a combination of the cricoid arytenoid cartilage and the internal arytenoid muscle in the anterior region, and by the cricopharyngeus and thyropharyngeus muscles in the posterior region. As food

passes through the upper sphincter, signals are transmitted to the brainstem's Instituut center, which initiates the sphincter's contraction. This action also involves a temporary stop in breathing to ensure that the food bolus moves smoothly. Structurally, the esophagus is composed of four layers: mucosa, submucosa, muscular (which has both longitudinal and circular muscle layers), and the outermost serosa. The coordination of the circular and longitudinal muscle layers helps reduce tension and enables the smooth movement of food.

Swallowing mechanisms differ between areas of the esophagus containing striated versus smooth muscles. Striated muscles are controlled by the ambiguous nucleus in the brainstem, which sends signals to initiate contraction. In contrast, smooth muscles are controlled by the dorsal nucleus of the vagus nerve, sending relaxation signals to allow the smooth muscles of the esophagus to relax, particularly in the lower part.

The lower esophageal sphincter, located at the entrance to the stomach, is a high-pressure area that does not possess a dilation mechanism. Food enters the stomach through the relaxation of the smooth muscles [14].

In individuals with Barrett's esophagus, there is an increased risk of developing adenocarcinoma, especially when additional risk factors such as obesity are present.

Esophageal stricture treatment

Esophageal strictures, whether malignant or benign, can often be managed endoscopically using a procedure known as stenting. Several types of stents are available, including self-expandable plastic stents (SEPS), self-expandable metallic stents (SEMS), and biodegradable stents. SEMS are typically constructed from materials like stainless steel, nitinol, or polymers coated with a silicone shell. However, a significant challenge with SEMS is the potential for stent migration, which can occur in 30-50% of cases. The selection of the appropriate stent involves six key testing procedures: compression force testing, expansion force testing, corrosion testing, tensile strength testing, deployment testing, and dimensional testing. One of the newer innovations in studying esophageal stenosis is the bio-mimicking robotic soft esophagus (RoSE), a promising technology. While the use of esophageal stents is beneficial for treating both malignant and benign strictures, and providing rapid symptom relief, complications like stent migration are common [15].

Symptoms of esophageal stenosis include difficulty swallowing (dysphagia), painful swallowing (odynophagia), aspiration, and chest pain. Chronic stenosis can result in weight loss and malnutrition. For benign esophageal strictures, the most frequent causes are peptic reflux, radiation therapy, caustic substances, Schatzki rings, and post-surgical scarring.

Endoscopic dilation is considered the primary treatment for esophageal strictures, with contraindications such as unhealed perforations, inability to sedate the patient, hemodynamic instability, or coagulopathy. Fluoroscopic guidance is typically used during stent placement, and when the superior approach is not feasible, a retrograde approach through the stomach may be employed. Both the balloon and spark plug dilation techniques are effective, with no significant difference in their outcomes. Dilation complications may include perforation, bacteremia, or bleeding, with perforation rates ranging from 0.1% to 0.6%, hemorrhage rates under 0.5%, and bacteremia occurring in 2-23% of cases. Guidelines generally do not recommend routine antibiotic prophylaxis. Approximately 80-90% of strictures can be successfully treated with dilation, although recurrence occurs in around 30% of patients [16].

Anatomically, simple strictures are short, focal, and linear, while complex strictures tend to be longer than 2 cm, irregular, or angulated, with a narrowed lumen.

Pharmacological treatments, such as steroid injections, aim to reduce inflammation and limit collagen formation. Mitomycin C is another agent used to minimize scar tissue after surgery. Additional approaches include surgical incisions for Schatzki rings and anastomotic strictures. Temporary stents have proven effective in maintaining an open lumen during the healing process and scar formation, with biodegradable stents being developed to eliminate the need for endoscopic removal [17].

Tissue engineering offers another potential treatment option for esophageal injuries, a technique that emerged in the 1990s. It integrates fields like molecular biology, medicine, and biochemistry to reconstruct tissue ex vivo and then implant it in vivo to repair damaged areas. Strictures are a common complication following esophageal surgery for neoplasms, and medications like Tranilast—an anti-allergic drug—can help prevent them by inhibiting collagen production and IL-6. Tranilast is more effective than endoscopic dilation for reducing stricture formation.

Currently, two primary tissue engineering techniques are in use. One involves applying an extracellular matrix along with a stent, while the second uses a thermo-responsive polymer for growing cell cultures. When the temperature is lowered, the cells detach while retaining their matrix, offering an advantage over enzymatic detachment methods [18].

Esophageal stenting and related treatment approaches

In situations where resources are limited, certain improvisations, such as the use of orotracheal tubes, have been employed as a palliative treatment with satisfactory outcomes [19]. Biodegradable stents are particularly beneficial, as they maintain radial tension for around 8 weeks. Their ability to naturally degrade eliminates the need for endoscopic removal, reducing both patient discomfort and the costs associated with surgery [20].

The concept of treating malignant esophageal strictures dates back to 1845 when a tube made from ivory was used for stenting. The first clinical trials took place in the 1960s and also focused on malignant strictures. Another indication for stenting includes esophageal leakage, which can lead to contamination of the mediastinum and potentially result in septic shock. The causes of esophageal leakage can either be malignant, such as tracheoesophageal fistulas, or benign, such as spontaneous leaks seen in conditions like Boerhaave's syndrome, or those arising from iatrogenic causes during procedures like endoscopy or after esophageal surgery [21].

For iatrogenic esophageal perforations, which are considered life-threatening, the traditional treatment approach involves surgery and drainage. However, recent advances have introduced esophageal stents as a viable alternative. These stents can be used temporarily to treat esophageal leakage, though the duration of their placement should be tailored to each patient's specific condition [22].

In some rarer cases, such as breast cancer metastasis to the esophagus, stenting may be required for palliative care. This procedure comes with similar risks of stent migration as in other conditions.

Esophageal perforation, although uncommon, is a serious and potentially fatal complication. It was first described by Hermann Boerhaave in 1724 after a series of vomiting episodes. In such cases, the stent serves to block bacterial entry, seal the perforation, and postpone the need for surgery, especially in hemodynamically unstable patients [23].

Regarding caustic ingestion, studies have shown that strictures develop in 3-57% of cases, with medical and dilation treatments proving effective in 64-100% of cases. For those who do not respond, more complex surgical interventions are required. In such instances, stenting may be kept in place for several weeks, with ongoing endoscopic monitoring to check for displacement [24-26].

Esophageal duplication is another rare condition, more commonly seen in children than adults. It can present in two forms: cystic (80% of cases) and tubular (20% of cases). If surgery to remove the cyst is not an option, using an endoprosthesis can be a highly effective method of managing the obstruction [27, 28].

In advanced esophageal cancers, treatments like radiotherapy and stenting are often used. Although complications are not fatal, they occur in around 28% of cases. The most common issues include chest pain (18.7%), stent occlusion (13.1%), tumor growth (9.7%), food blockage (3.4%), reflux (9.4%), cough (5.7%), nausea and vomiting, mild bleeding (3.1%), and aspiration pneumonia. Mispositioned stents and failure to expand properly occur in 2.9% and 2.6% of cases, respectively [29-31].

Conclusion

Both malignant and benign esophageal strictures can be effectively managed through the endoscopic procedure of stenting. Stents can be made of various materials, including metal, polymer, or biodegradable substances. The primary challenge with stenting is the risk of stent migration. The first known attempt at stenting occurred in the 19th century using an ivory tube. For caustic substance ingestion, dilation and stenting yield highly successful results. Complications can occur both immediately and over time, ranging from pain to failure in stent expansion.

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