

Evolving Endoscopic Techniques In The Management Of Gastrointestinal Tumors

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Introduction: The lines between non-invasive medical treatments and invasive surgical treatments meet at therapeutic endoscopy. Advances in endoscopic practice are challenging traditional views on how neoplasia should be managed in the gastrointestinal system. Identifying pre-malignant changes in the gut is central to successful early management of most cancers. There has been rapid growth in the equipment and technology available for evaluating potentially neoplastic lesions in the gastrointestinal tract. Not only tumors have gotten the premium interest but also non oncologic diseases were also involved. The model of an endoscopist has changed in the last 10 years. Nowadays, the endoscopist has to be skillful not only in using standard endoscopes and macroscopic view of the lesions in the gut but with good experience in ultrasound, pathology and physics. Since 1961, the conventional white light fiber endoscopes have been and still mainly used for the diagnosis of mucosal lesions with the ability of many diagnostic and therapeutic interventions. However, no detailed information can be obtained about the mural layers of the gut and extramural organs.

Electronic Videoendoscopes:

Electronic videoendoscopes emerged with CCD of 100-300K pixel allowed more pixel density and better resolution than fiberoptic endoscopes.

High resolution endoscopes and magnification endoscopes:

High resolution endoscopes are second generation electronic videoendoscopes with 850K pixel density and higher resolution than previous generations. This high resolution allows the detection of lesions and discrimination of details that could be missed by lower resolution endoscopes. Some high resolution endoscopes are equipped with an optical zoom facility comprising of a movable motor driven lens in the tip of the scope. By controlling the focal distance, the scope can move very close to the mucosal surface providing the magnified image.

These scopes are referred to as magnifying endoscopes. Optical magnification is very closely related to the concept of high resolution. At the same level of magnification, a high resolution endoscope will provide a more detailed picture than an optical magnifying endoscope. The image resolution of the latter can be improved to the level of the high resolution scope by optically increasing the level of magnification at the expense of reducing the surface area that is visualized. Here lies probably one of the most promising aspects of use of high resolution endoscopes: the superior ability to discriminate detail in the non-magnified overview image. Such property is a key requirement of a

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screening tool: before a suspicious small lesion can be scrutinized and discriminated (by magnification endoscopy and chromoscopy) it must first be detected. Image manipulation with an electronic zooming (magnification) facility is sometimes confused with optical magnification. There is, however, an important distinction. Electronic magnification can provide a more detailed image of a lesion, but only up to a certain level. Image quality is lost at some point because with every step of electronic magnification the image is composed of fewer pixels as compared with optical magnification.

Chromoendoscopy:

Chromoendoscopy involves the topical application of stains or pigments to improve tissue localization, characterization, or diagnosis during endoscopy. The images obtained by magnification endoscopy can be further enhanced by the topical application of stains or pigments (enhanced magnification endoscopy or magnification chromoscopy). Chromoendoscopy has been used in the evaluation of Barrett esophagus, esophageal adenocarcinoma, gastric metaplasia, adenocarcinoma, colon polyps, colon cancer and surveillance in inflammatory bowel disease. This technique is still underused in most countries except Japan. This seems unjustified given the fact that the equipment needed is readily available and cheap, the technique is not difficult to learn, and with some experience adds only a little extra time to the procedure. Agents used for chromoscopy are categorized according

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to several agents have been described that can broadly be categorized as absorptive (vital) stains, contrast stains, and reactive stains. Their working principle: Vital stains like Lugol's solution and methylene blue are absorbed into the cells. Contrast stains like indigo carmine are not absorbed but accumulate in pits and valleys between cells highlighting mucosal architecture. Reactive stains like Congo red and phenol red react to changing conditions of acid secretion and carry a potential with regard to the early detection of gastric cancer and *Helicobacter pylori* infection. Lugol's solution contains potassium iodine and iodine that reacts with glycogen in non-keratinized squamous epithelium. Normal squamous epithelium stains deeply brown giving the oesophagus a snake skin-like appearance while areas with inflammation, dysplasia, or (early) cancer lack appropriate staining because of a depletion of glycogen.

Narrow band image (NBI):

NBI is an optical filter technology that radically improves the visibility of capillaries, veins and other subtle tissue structures, by optimizing the absorbance and scattering characteristics of light. NBI uses two discrete bands of light: One blue at 415nm and one green at 540nm. Peak light absorption of hemoglobin occurs at those wavelengths and blood vessels appear dark, allowing for their improved visibility. Narrow band blue light displays superficial capillary networks, while green light displays subepithelial vessels and when combined offer an extremely high contrast image of the tissue surface. NBI has found use in the identification of Barrett esophagus, atypical dysplastic cells in the colon of patients with ulcerative colitis and the pit pattern classification of colorectal polyps and tumors.

Confocal laser (CLE):

Confocal laser endomicroscopy, a recent advance of endoluminal imaging, allows *anin-vivo* visualization and study of mucosal layer to a micron resolution to give an optical biopsy with a detailed visualization of tissue and subcellular structures. CLE has the potential to anticipate the final diagnosis (neoplastic vs. non-neoplastic) and consequently to guide next therapeutic steps in clinical practice without the delay of a pathology response. Indeed one of the fundamental features of endoscopic procedures consists in the possibility to perform direct biopsies in order to achieve histological diagnosis. Although histology is highly accurate, it has few limitations: false negative results, delay in reaching the final diagnosis and the decision of the correct and best treatment and increased costs in pathology procedures with, consequently, the need of repeated procedures. Also biopsy is responsible for fibrosis at the site of biopsy with consequent difficulty in evaluation for possible mucosectomy.

CLE has been used with high sensitivity and specificity in visualization of intestinal metaplasia, dysplasia, and malignancy in Barrett esophagus. The conventional repeated biopsies are time wasting, randomly allocated and cause fibrosis that render endoscopic therapeutic

mucosectomy difficult. CLE has been used similarly in the detection of early gastric cancer, surveillance in inflammatory bowel diseases and the differentiation of hyperplastic from dysplastic colorectal polyps.

Endoscopic ultrasound:

Endoscopic ultrasound has been used successfully in the diagnosis and staging of gastrointestinal tumors. The passage of endoscopes with ultrasonographic probes fitted over the tip allowed the study of the full thickness of the wall of the upper and lower gastrointestinal tract and the extra-luminal organs and lymph nodes.

The development of new therapeutic endoscopic maneuvers was necessarily preceded by a comparable advance in diagnostic endoscopic techniques. Endoscopic mucosal resection and submucosal dissections are advanced endoscopic interventions that evolved based on the novel diagnostic endoscopes.

Endoscopic mucosal resection (EMR):

The risk of nodal spread is increased more than 5 times when gastrointestinal tumors spread beyond the mucosa. Endoscopic mucosal resection (EMR) is a technique used for the staging and treatment of superficial neoplasms of the gastrointestinal tract. The depth of invasion and the decision for the procedure can be accomplished using traditional biopsies, EUS, and with the aid of other challenging techniques like narrow band imaging, Chromoendoscopy, high resolution endoscopy, magnification endoscopy and confocal laser endoscopy.

Indications:

- The technique is used with great success in the management of Barrett esophagus with dysplasia or early adenocarcinoma.
- Early gastric cancer
- Ampullary and non-ampullary duodenal adenoma, early adenocarcinoma and ampullary submucosal lesions
- Colonic laterally spreading benign tumors, flat polyps and early adenocarcinoma.

The concept of this technique is to resect the mucosal lesion using electric current after creating cushion effect with submucosal injection of saline. Mucosal non-lifting after submucosal injection is an accurate and specific predictor of submucosal invasion. Mucosal resection can be done by the traditional polypectomy snare, cap and snare polypectomy or using band ligation technique in resection.

Complications:

Bleeding (1.5-2%) is immediate, or delayed after 24 hours and rarely after 5-7 days. The condition is usually self limited but sometimes local endoscopic treatment may be needed. Epinephrine injection, argon coagulation, and endoclips are all methods of hemostasis but rarely laparotomy may be required.

Perforation (0.05-2%) usually occurs when resection extends to the serosa. Immediate surgical consultation and exploratory laparotomy may be needed.

Transmural burn injury (1%) occurs when the electric current extends to the serosa. The condition usually resolves with conservative management.

Endoscopic submucosal dissection (ESD): ESD has been developed from one of the EMR techniques as a reliable en block dissection of GI neoplasms. ESD differs from EMR, in the former no snares are used but electric knives. Major advantages of this technique in comparison with EMR are as follow. The resected size and shape can be controlled unlike EMR which depend on the cap and snare used and en block dissection is possible even in large neoplasms. In Japan ESD is accepted as the standard therapy for early gastric cancer especially large or ulcerative lesions. Recently, ESD is applied to esophageal and colorectal neoplasms. In Japan, for early gastric cancer 3-years disease free survival rate was 90%-92%). In esophageal ESD the 3-years survival rate ranged from 86%-95%)

Complication:

Perforation is the most serious complication (1.5-12%) and can be small and successfully managed by sealing with endoclips and conservative management. However, larger perforation is managed by surgical laparotomy. Other complications like bleeding, pain and stricture formation can also occur in esophageal and pre-pyloric lesions. The main challenge to ESD is it requires a highly skilled endoscopist with a multi-specialty team.

Further refinement of ESD is needed to permeate this technique and popularize it as a safe and effective treatment modality for GI neoplasms.

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