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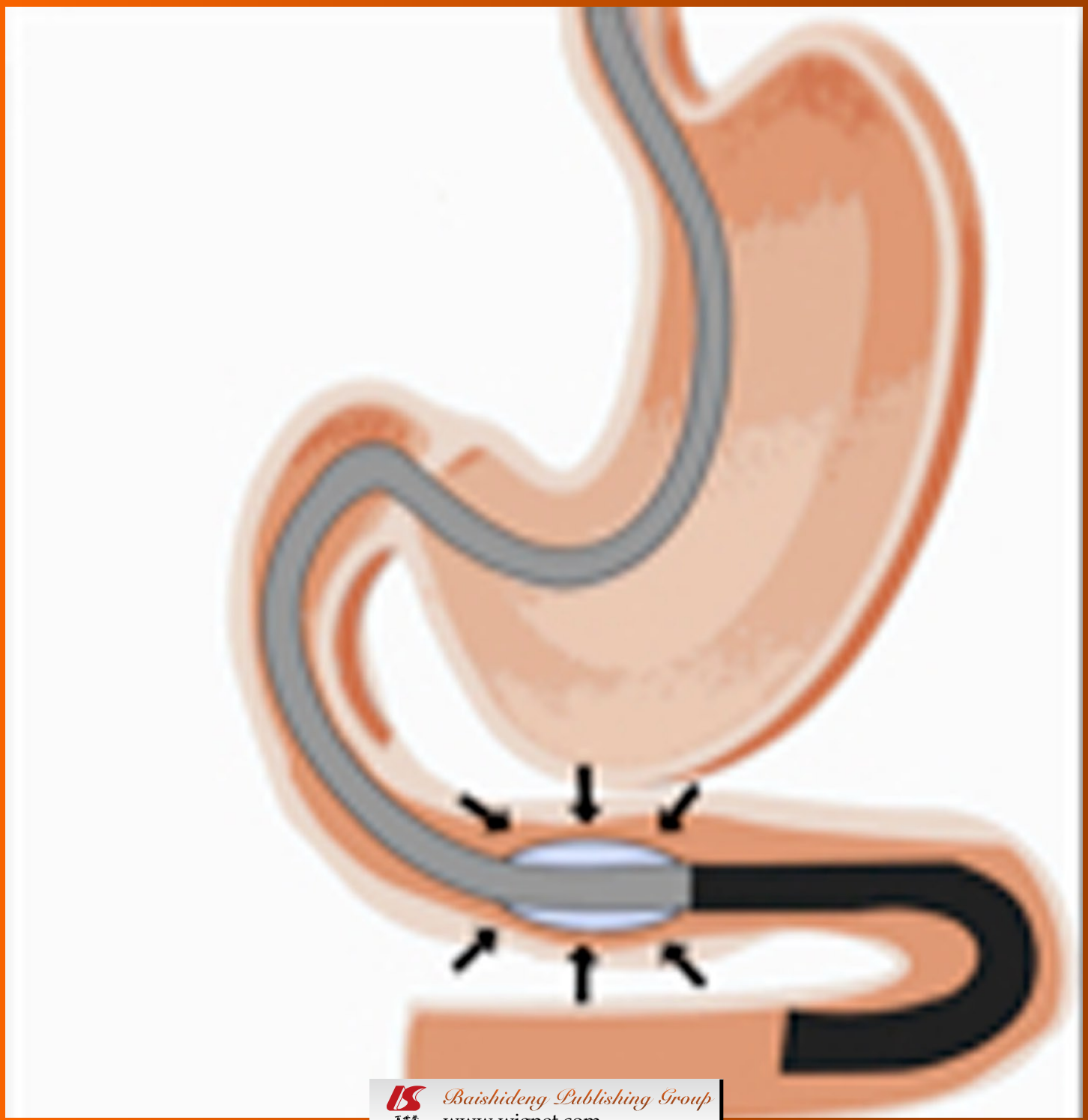

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Contents

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EDITORIAL

High technology imaging in digestive endoscopy

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Abstract

A thorough endoscopic visualization of the digestive mucosa is essential for reaching an accurate diagnosis and to treat the different lesions. Standard white light endoscopes permit a good mucosa examination but, nowadays, the introduction of powerful endoscopic instrumentations increased ability to analyze the finest details. By applying dyes and zoom-magnification endoscopy further architectural detail of the mucosa can be elucidated. New computed virtual chromoendoscopy have further enhanced optical capabilities for the evaluation of submucosal vascolar pattern. Recently, confocal endomicroscopy and endocytoscopy were proposed for the study of ultrastructural mucosa details. Because of the technological contents of powerful instrumentation, a good knowledge of implemented technologies is mandatory for the endoscopist, nowadays. Nevertheless, there is a big confusion about this topic. We will try to explain these technologies and to clarify this terminology.

Key words: HDTV; Zoom endoscopy; Magnifying endoscopy; Fujinon intelligent color enhancement; Narrow band imaging; I-scan; Confocal laser endoscopy; Endocytoscopy

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INTRODUCTION

The need of an ever-growing earliness in detection of digestive malignant lesions has led the endoscopy onto a new high-technology course through the development of the so-called powerful endoscopy. Keeping pace with the rapid developments in technology, the optical features of these new powerful endoscopes offer a resolution that allows the visibility of new surface details.

The new powerful digestive endoscopy enables to perform high-resolution endoscopy, high-magnification endoscopy (magnifying or zooming), computed virtual chromoendoscopy (CVC), confocal laser endoscopy (CLE), and endocitoscopy.

Some of these techniques increase diagnostic performances through resolution improvement, while other techniques through modifying the chromatic spectrum of the endoscopic picture. In some cases the augmented vision is due to the charge coupled device (CCD) features, in some other is due to the features of the central processor unit (CPU).

Because of the specific contents of powerful instrumentation, a good knowledge of implemented technologies is mandatory for the endoscopist, nowadays. Nevertheless, there is a big confusion about the technological terminology, despite the number of papers on the matter that are, sometimes, inaccurate. In this editorial, we will try to explain the technologies implemented in powerful

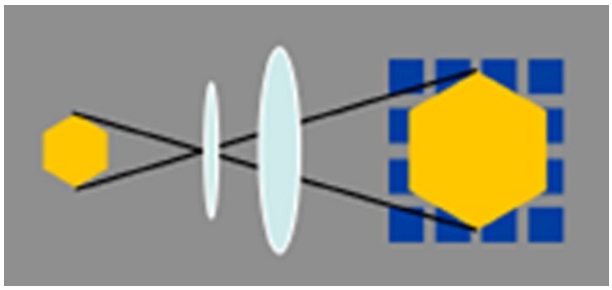

Figure 1 Zoom endoscopes perform optical zoom by using a movable lens in the tip of the endoscope: This system provides a closer image of the target while maintaining image display resolution.

Figure 2 Electronic magnification simply moves the image closer on the display and results in a decreased number of pixels composing the area of display, with no improvement in resolution.

endoscopes, clarifying some terms often abused, sometimes misused.

HIGH-RESOLUTION AND HIGH MAGNIFICATION ENDOSCOPY

The video capabilities of color images of standard definition (SD) endoscopes are based on traditional television (TV) broadcast formats[1,2]. The SD signals offer images in a 4:3 aspect ratio, with image resolutions of 640 to 700 pixels width by 480 to 525 pixels or "lines" height (approximately 367.000 pixels)[2]. SD endoscopes are equipped with CCD chips that produce an image signal of 100 000 to 400 000 pixels, which are displayed in the SD format. Advances in CCD technology have resulted in smaller CCDs with an increased number of pixels and increased resolution. The CCDs used in current so-called high-resolution or high-definition (HD) endoscopes produce signal images with resolutions ranging from 850 000 pixels to more than 1 million pixels.

A HD and high resolution image is generally defined as having a resolution higher than 650 to 720 lines (height)[3]. Moreover, images may be progressive or interlaced. With progressive (p) images, lines are scanned consecutively and the image is painted 60 times per second, whereas with interlaced (i) images, every other line is scanned and the image is painted in 2 passes at 30 times per second each.

HD video imaging can be displayed in either TV or computer monitor formats. The 16:9 aspect ratio is not useful to display images from round endoscopic lenses. Traditionally, endoscopic images are displayed in a 4:3 aspect ratio to match the standard aspect ratios of SD TV and because this ratio provides the highest pixel density and resolution possible given the lens shape. Display in computer monitor formats use progressive scanning and is not restricted by broadcast HD formats or aspect ratios. Monitors had traditionally 4:3 aspect ratios but recently 5:4 ratios have become more popular. Current high resolution endoscopic CCDs display images in either 4:3 or 5:4 aspect ratios[3].

It is important to recognize that, to provide a true HD image, each component of the system (e.g., the endoscope CCD, the processor, the monitor, and transmission cables) must be HD compatible. Three different high-resolution endoscope systems are currently commercially available: (1) Olympus high-resolution endoscopes are designed based on the commercial availability of TVs and recorders for output onto HDTVs. The output from the endoscope is enhanced to 1080i; however, the endoscopic image itself is displayed within a 1280 × 1024-pixel frame; (2) Fujinon high-resolution endoscopes are designed for output onto computer monitors. The first Fujinon CCD chips were 1077 × 788 pixels and their output was equivalent to XGA monitors[2]; however, current endoscopes have an output of 1280 × 960 pixels. The actual resolution of the CCD is proprietary. The latest processors enhance the image to 1080 i; and (3) Pentax Medical high-resolution endoscopes are designed for output onto computer monitors. The Pentax CCD provides 1280 × 1024 pixels and displays at native resolution.

High-resolution endoscopes magnify the endoscopic images 30 to 35 times. Zoom endoscopes are defined by the capacity to perform optical zoom by using a movable lens in the tip of the endoscope[4]. The optical zoom provides a closer image of the target while maintaining image display resolution (Figure 1). This is distinguished from electronic magnification, which simply moves the image closer on the display and results in a decreased number of pixels composing the area of display, with no improvement in resolution (Figure 2)[5]. With a suitable processor, conventional endoscopes provide an electronic magnification of 1.5 to 2. Although standard endoscopes magnify images 30 to 35 times, zoom endoscopes can optically magnify images up to 150 times, depending on the size of the monitor.

COMPUTED VIRTUAL CHROMOENDOSCOPY

CVC is a real-time, on-demand endoscopic imaging technique that, adjusting the spectroscopic characteristics of the videoendoscopic systems through a frame sequential lighting method[6], allows to enhance visualization of the vascular network and mucosal surface texture in an effort to improve tissue characterization, differentiation, and diagnosis. CVC is considered a potential alternative to traditional chromoendoscopy, providing contrast en-

hancement of tissue surface structures, although it has not been studied as extensively as chromoendoscopy. Three different CVC systems are now commercially available: the Olympus Narrow Band Imaging (NBI), the Fujinon Intelligent Color Enhancement (FICE), and the Pentax iScan.

Standard videoendoscope systems use the entire spectrum of visible light (400-700 nm). These white-light imaging endoscopic systems are designed to simulate daylight, thus allowing examining the tissues in their natural colors. This kind of videoendoscopic images can be obtained by one of two different systems: red-green-blue (RGB) sequential and color CCD[7].

In the RGB sequential system, the light from a xenon arc lamp is filtered through a rotating broadband RGB filter located between the lamp and the endoscope's light guide in order to obtain sequential bursts of red, green, and blue light that give rise to the visual strobe effect. After tissue illumination, the reflected red, green, and blue tissue images are sequentially captured by a monochromatic CCD at the tip of the endoscope and transmitted to a video processor. The 3 images are fed into the electron guns that illuminate respectively the red, green, and blue phosphor dots on the monitor to create a final composite image in full natural color[8].

The color CCD system use a micromosaic color filter mounted over the CCD itself. Continuous white-light illumination from the xenon lamp is delivered to tissue by the endoscope's light guide, and the reflected light and image created on the CCD surface is then processed by circuitry in the video processor before display. Similar to the RGB system, tissue structures that heavily reflect the red, green, and blue light are displayed on the R, G and B video channels on the video monitor, respectively[8].

The NBI system (Olympus Medical Systems, Tokyo, Japan) emphasizes the mucosal microvasculature and is able to identify vascular alterations indicating pathologic conditions[9-12]. In the NBI system, narrow bandpass filters are placed in front of a conventional white-light source in order to produce a contrast between vascular structures and the surrounding mucosa.

When compared to the initial 3-band NBI prototypes, currently available NBI systems use just 2 different narrow band filters[8]: (1) The first filter provides tissue illumination in the blue spectrum of light at 415 nm, emphasizing capillaries in the superficial mucosal layer and showing them in brown; and (2) The second filter provides tissue illumination in the green spectrum of light at 540 nm; this wave-length corresponds to the secondary hemoglobin absorption peak, and emphasizes deeper mucosal and submucosal venular vessels displaying them in cyan.

The NBI system can be coupled with electronic or optical (zoom) magnification for enhanced visualization of mucosal details. The FICE system (Fujinon, Saitama, Japan) is merchandised as a digital image processing technique enhancing the mucosal surface structures by using selected wavelengths of light in reconstituted virtual images.

Unlike NBI (that uses optical filters), the FICE system is software-driven and uses an image processing algorithm that is based on spectral estimation methods. In this technology, developed by professor Yoichi Miyake[13], a standard image captured by a color CCD videoendoscope is sent to a spectral estimation matrix processing circuit contained in the EPX 4400 video processor. Here, the various pixels spectra corresponding to the conventional image are mathematically estimated. Because the pixels spectra are well known, it is possible to implement imaging on a single wavelength. Such single-wavelength images are randomly selected, and assigned to red, green and blue respectively, to build and display a CVC-enhanced color image. The digital processing system is able to switch between an ordinary image to a FICE image immediately simply pressing a button on the handle of the endoscope. It is possible to select the most suitable wavelengths for examination because of the system's variable setting functions, with up to ten preselect settings.

These ten presets can also be customized and configured from a very large number of wavelength permutations, because any of 60 wavelengths (400 to 695 nm, in increments of 5 nm) can be input into any of the 3 (RGB) channels[14]. A push button on the handle of the endoscope can be programmed to enable switching between the conventional white-light image and the corresponding FICE image of a single specified preset.

The FICE system can also be coupled with electronic or optical (zoom) magnification for enhanced visualization of mucosal details. iScan (Pentax, Tokyo, Japan) is the latest CVC technology developed and is merchandised as a digital contrast method among endoscopic imaging techniques[15].

This CVC system has three modes of image enhancement: (1) Surface Enhancement (SE) enhances the structures through recognition of the edges; (2) Contrast Enhancement (CE) enhances the depressed areas and differences in structure through colored presentation of low density areas; and (3) Tone Enhancement (TE) enhances individual organs through modification of the combination of RGB components for each pixel.

SE and CE are possible switching between three enhancement levels (low, medium and high). TE is possible switching between three objects (esophagus, stomach and colon). The three modes (SE, CE and TE) are arranged in series, therefore, it is possible to apply two or more of these three modes at one time. Switching the levels or modes of enhancements can be done on a real-time basis, without any time lag by pushing a button, thus enabling an efficient endoscopic observation[16].

With SE, the difference in luminance intensity between the pixels concerned and the surrounding pixels is analyzed and the edge components are enhanced. With ordinary enhancement, minor changes in structure can be perceived as noise. Adjustment of the noise erasure function allows more evident enhancement of the edg-

es[17]. When compared to normal images, SE images do not differ in brightness and differ little in color.

With CE, areas of lower luminance intensity are compared to surrounding pixels and identified on the basis of pixel-wise luminance intensity data, followed by relative enhancement of the B component through the slight suppression of R and G components in the low luminance area. As a result of CE, the low luminance area is stained in slightly bluish white, and minute irregularities on the mucosal surface are enhanced[18]. This images processing do not cause a change in image brightness or a marked change in the color of the images. It causes only a slight bluish-white staining of depressed areas.

With TE, the RGB components of the endoscope image are disintegrated into each component (R, G and B) which are converted independently along the tone curve, followed by a re-synthesis of the three components in order to yield a reconstructed image. The tone curve is depicted by plotting input (on the x axis) against output (on the y axis). The tone curve can be changed into various forms, by modifying of the parameters, into S and J types. If the tone curve assumes an S type, the high R-component area is shifted to a further higher range of R to enhance the color tone R, or the low R-component area is shifted to a further lower range of R to elevate the sensitivity to GB components, thus allowing clear enhancement of the differences in color tone. If the tone curve assumes a J-type form, the R component is shifted completely to a low R range, to elevate the overall sensitivity to GB components and the brightness/darkness contrast[16-19].

In conclusion, there have been no reported complications attributed to the use of NBI, FICE or iScan[8]. The costs of endoscope systems supplied with CVC is higher than those with white light but no formal cost analyses have been reported on this topic. Moreover, there are no unique CPT* (Current Procedural Terminology) codes for NBI, FICE or iScan[8].

CONFOCAL LASER ENDOSCOPY

CLE is a new endoscopic technology, developed to obtain high-resolution images of gastrointestinal mucosa, based on tissue illumination with a low-power laser with subsequent detection of the fluorescence light reflected from the tissue through a pinhole[20]. The term *confocal* refers to the alignment of both illumination and collection systems in the same focal plane[21]. The laser light is focused at a selected depth in the tissue of interest and reflected light is then refocused onto the detection system by the same lens. Only the returning light refocused through the pinhole is detected. The light reflected and scattered at other geometric angles from the illuminated object or refocused out of plane with the pinhole is excluded from detection[22]. This dramatically increases the image resolution, providing almost a histological examination, a kind of optical biopsy, of the superficial layer of the digestive tract[23-25]. Confocal imaging can be based on tissue reflectance or tissue fluorescence. The confocal devices based on tissue reflectance do not require any contrast agents, but have many technical problems and low resolution, compromising clinical utility[24,26]. Whereas, confocal endomicroscopy based on tissue fluorescence uses local and/or intravenous contrast agents and generates high-quality images comparable with traditional histology[27,28].

Two kind of confocal endoscopes are today commercially available. The first model is integrated into the distal tip of a conventional upper endoscope (EG-3870CIK; Pentax, Tokyo, Japan) or colonoscope (EC-3870CILK; Pentax). The second type uses a dedicated confocal miniprobe with laser microscope (Mauna Kea Technologies, Paris, France) inserted through the accessory channel of a traditional endoscope. All these instruments have CE code and US Food and Drug Administration authorization and provide different depths of imaging, field of views, and lateral resolutions.

The Mauna Kea confocal gastro-intestinal miniprobes include CholangioFlex, GastroFlex (standard and UHD) and ColoFlex (standard and UHD). All probes generate dynamic images, with 12 frames per second and are reusable approximately for 20 studies. The depth of imaging is 40 mm to 70 mm for CholangioFlex probes, 70 to 130 mm for GastroFlex and ColoFlex probes, and 55 to 65 mm for GastroFlexUHD and ColoFlexUHD probes. The maximal field of view is 325 mm for CholangioFlex probes, 600 mm for GastroFlex and ColoFlex probes, and 240 mm for GastroFlexUHD and ColoFlexUHD probes. The lateral resolution is 3.5 mm for CholangioFlex, GastroFlex, and ColoFlex probes, and 1 mm for GastroFlexUHD and ColoFlexUHD[29,30].

The Pentax confocal microscope integrated into the conventional endoscopes acquires images at a scan rate of 1.6 frames per second (1024 × 512 pixels) or 0.8 frames per second (1024 × 1024 pixels) with an adjustable depth of scanning ranging from 0 mm to 250 mm, a field of view of 475 × 475 mm, a lateral resolution of 0.7 mm, and an axial resolution of 7 mm[31,32].

The fluorescent contrasts for CLE can be administered intravenously or topically. Intravenous fluorescein (Pharmalab, Lane Cove, New South Wales, Australia) distributes throughout the extracellular matrix of the surface epithelium and lamina propria but does not stain cell nuclei[21]. Topically administered acriflavin (Sigma Pharmaceuticals, Clayton, Victoria, Australia), tetracicline or cresyl violet (AnaSpec, Inc, San Jose, CA, United States) stains cell nuclei of the surface epithelium but does not penetrate to deeper layers of the mucosa[21]. Acriflavin is a mutagenic dye and a potential human carcinogen, which will likely limit its clinical utility[33]. After the contrast administration, the tip of the confocal endomicroscope or miniprobe is positioned in gentle contact with the area of interest to obtain high-resolution confocal images. Accumulated images can be saved for postprocedural analysis.

ENDOCYTOSCOPY

Endocytoscopy (EC) is an ultra magnification technique providing images of surface epithelial structures at cellular resolution[34-36]. This technique is based on the contact light microscopy principle leading to real-time visualization of the cellular structures of the superficial epithelial layer. The technology uses a fixed-focus, high-power objective lens projecting onto a CCD very highly magnified images from a 0.5 mm diameter sample.

Currently we have two kind of EC instruments, both manufactured by Olympus (Tokyo, Japan) and available only as prototype devices: (1) The probe-based instrument consists of 2 flexible devices providing ultra-high magnification images of the epithelial surface at 570x or 1400x on a 19-inch monitor (or 450x and 1125x on a 14-inch monitor); these probes are realized to fit through therapeutic channel of endoscopes (minimum 3.7 mm) and necessitate contact with the tissue surface for imaging[37]; and (2) The endoscope-based instrument integrates the EC component within the endoscope. Both the upper (103 cm long) and lower (133 cm long) prototype provide an image magnification of 580x on a 19-inch monitor, in addition to having conventional optical magnification and narrow-band imaging capabilities. The tip of the endoscopes is placed in contact with the tissue surface to generate endocytoscopic images[38].

Endocytoscopic visualization necessitates treatment of the mucosa with a mucolytic agent, such as N-acetylcysteine, and prestaining with an absorptive agent, such as methylene blue (0.5%-1%) or toluidine blue (0.25%). Excess staining is washed off before imaging[39]. EC-based image criteria for tissue diagnosis and/or classification in the esophagus, stomach, and colon have been described, but not yet validated prospectively[40-42].

CONCLUSION

The frontiers of endoscopy continue to widen: the development and the implementation of new technologies in endoscopic instrumentation is a challenge that we seem to have won. Nevertheless, as the experience teaches us, not all of these technologies will be ultimately integrated into the practice of digestive endoscopy. Some technologies are still experimental or in the proof-of-concept stage, and some will have a story of failure or prolonged stagnation of promising concepts. Just a few will become viable, showing an important impact on diagnosis and treatment of digestive diseases.

However there is no doubt that this new course of gastro-intestinal endoscopy requires knowledge and mastery of implemented technologies and their specific terms. The new endoscopist will probably find himself closer to the engineering, IT, and technical environment.

We are sure that our professional category, the scientific societies and journals may play an important role in organizing a formalized program aimed at supporting the approach to technological innovation in endoscopy.

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OBSERVATION

Single balloon enteroscopy: Technical aspects and clinical applications

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Abstract

The small bowel has long been considered a black box for endoscopists because of its long length and the presence of multiple complex loop. Most of the small bowel is inaccessible by traditional endoscopic means. In addition, radiographic studies have significant limitations with regard to diagnostic yield, and surgery is an invasive alternative. This limitation was overcome through the development of balloon enteroscopy that becomes established throughout the world for diagnostic and therapeutic examinations of the small bowel. The single-balloon enteroscope (SBE) system (Olympus, Tokyo, Japan) was introduced into the commercial market in 2007. Several study demonstrated its efficacy and safety. Early reports on the use of single-balloon enteroscopy have suggested a high diagnostic yield and similar therapeutic potential to that of the double-balloon endoscope. SBE is viable technique for in the management of small bowel disease. Technically, it is easy to perform, may be efficient, and in the literature data available, seems to provide high diagnostic and therapeutic yield.

Key words: Single balloon enteroscopy; Small bowel; Enteroscopy

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INTRODUCTION

The small bowel has long been considered a black box for endoscopists because of its long length and the presence of multiple complex loop. Endoscopy using standard gastroscopes can reach up to the second or third portion of the duodenum while push enteroscopy can reach the ligament of Treitz and approximately about 80 cm beyond. Colonoscopy can reach 10 cm to 20 cm beyond the ileocecal valve. Most nonsurgical endoscopic techniques were unsatisfactory, and managing small-bowel diseases often required surgical intraoperative enteroscopy. Thus, the development of capsule endoscopy (CE) and double-balloon enteroscopy (DBE) has permitted the observation of the entire small bowel. The diagnostic yield of the balloon-enteroscopy for relevant pathologic findings can be of 70%-80%; in addition, it allows histologic sampling and endoscopic therapy that

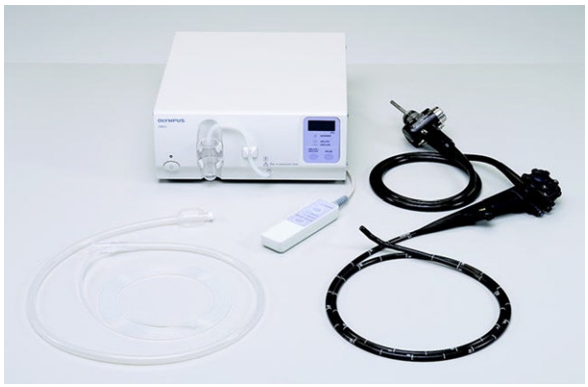

Figure 1 Single-balloon enteroscope system by Olympus.

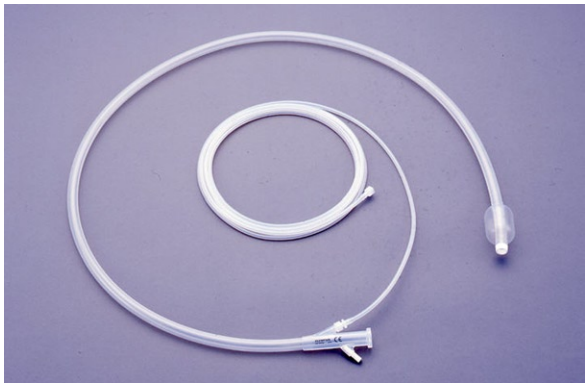

Figure 2 Disposable silicone splinting tube with balloon (ST-SB1).

it can be performed in more than 50% of patients.

SINGLE-BALLOON ENTEROSCOPE SYSTEM

The single-balloon enteroscope (SBE) system (Olympus, Tokyo, Japan) was developed in 2006 and was introduced into the commercial market in 2007. It is easier to use respect to double-balloon enteroscope, avoiding attaching the enteroscope balloon to the distal tip of the scope encountered and the requirement of inflating and deflating two balloons.

The single-balloon enteroscope system consists of the SIF-Q180 enteroscope, an overtube balloon control unit (OBCU Olympus Balloon Control Unit) and a disposable silicone splinting tube with balloon (ST-SB1) (Figures 1-3).

The enteroscope is a high-resolution video endoscope that works with Olympus EVIS processors and EVIS EXERA II system. The outer diameter is of 9.2 mm with working length of 2000 mm, while the operating channel size is of 2.8 mm.

The splinting tube is an overtube with an inflatable balloon fixed to the distal, radiopaque tip, both in latex-free silicone. The inner diameter of the tube is 11 mm, the outer diameter is 13.2 mm, the working length is 1320 mm, and the total length is 1400 mm. The addition

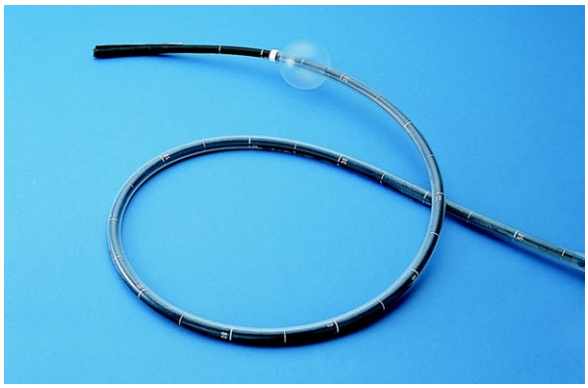

Figure 3 Single-balloon enteroscope with overtube.

of a small amount of water through a small port on the proximal end of the splinting tube activates the hydrophilic coating avoiding friction between the overtube and the enteroscope. Additional water can be flushed into a dedicated port throughout the procedure, in order to reduce friction or to wash away debris collected between the enteroscope and the splinting tube. The balloon is inflated and deflated by a balloon control unit with a safety pressure setting range from -6.0 kPa to +5.4 kPa. The overtube balloon control unit has one button for inflation, one button for deflation, and a third control for the pause/cancel feature.

TECHNICAL ASPECTS

No bowel preparation is generally recommended in most cases for single-balloon enteroscopy by the oral approach, except a minimum of 12 h fasting while the standard 4 L of a polyethylene glycol (PEG) preparation is used for retrograde approach.

For retrograde SBE, conscious sedation as for colonoscopy is sufficient in most cases. For anterograde approach deep monitored sedation with propofol or general anesthesia with intubation is recommended[1].

Because of length of the procedure, large volumes of air are usually insufflated that can lead to failure of the procedure. Carbon dioxide (CO_2), unlike standard air, is rapidly absorbed from the bowel. A randomized, double blind trial showed that insufflation with CO_2 is safe, reduces patient discomfort, and significantly improves intubation depth[2,3].

Fluoroscopy can be helpful during the initial 10 to 20 SBE cases to observe advancement and reduction of the enteroscope and as an aid to determine when looping is present and how to solve it.

In addition, for some patients with surgically modified anatomy and for those undergoing therapeutic procedures such as dilations, fluoroscopic guidance is recommended.

Technique for anterograde approach

There are two techniques in order to advance the enteroscope into the small bowel that can be alternately used in

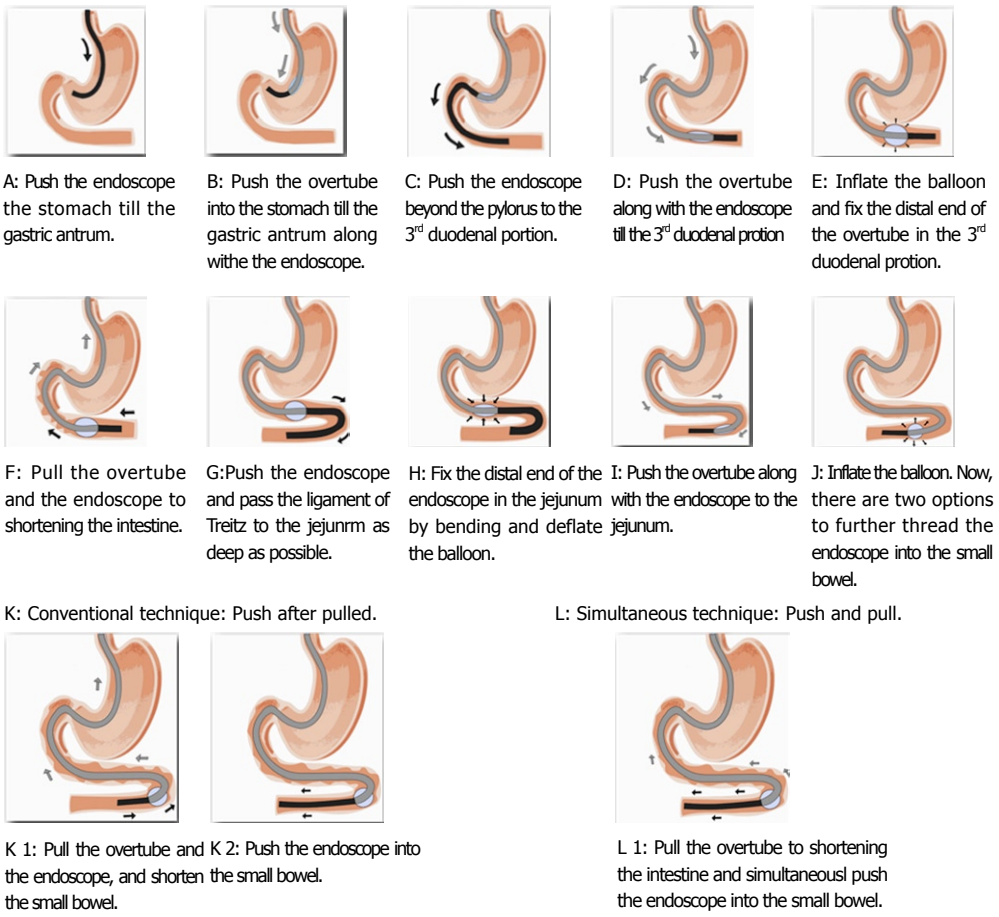

Figure 4 Representative scheme of single-balloon enteroscopy techniques.

the same exam. With the "conventional technique", the enteroscope is initially passed into the esophagus with the same technique used for a standard gastroscopy. The enteroscope is pushed into the duodenum until lacking of forward advancement. By angulating the tip of the enteroscope in order to hook the intestine, the overtube is gently advanced over the enteroscope to the point of maximal insertion, located at 155 cm, where a white line is present on the scope. In order to shorten the intestine and to advance into the small bowel, the endoscope and the overtube, with inflated balloon, are withdrawn together. Then, the endoscope is pushed maximally into the small bowel. The balloon still inflated allows the pushing force of the operator applied to the endoscope to be transmitted to the distal end of the endoscope without further stretching of the intestine. The repetition of these manoeuvres permits progression of the endoscope (Figure 4)[4].

Hartmann and colleagues[5] described an alternative method of single-balloon enteroscopy insertion ("simultaneous" technique) that consists of withdrawing only the inflated overtube in order to shorten the intestine, and simultaneously pushing the endoscope as deep as possible into the small bowel. In a study published by author and his colleagues[6], the alternative technique allowed a lower mean procedure time while the depth of insertion did not differ significantly between the conventional and alternative techniques.

To estimate the depth of insertion, the method proposed by May *et al*[7] can be used, recording data on a standardized documentation sheet. This method was validated with an animal model during training courses and demonstrated to be accurate. For each advancement of the enteroscope, the distance is added, usually ranging between 20 cm and 40 cm. Any portion of an advancement that is lost during a reduction manoeuvre is then subtracted.

When advancement is no longer possible, it is recommended to mark the area with a tattoo of India ink, injected with a sclerotherapy needle, or to position a clip. This marker can then be visualized during subsequent balloon-assisted enteroscopy performed with the opposite approach.

Once the point of maximal insertion is reached, the enteroscope can be gradually withdrawn. The overtube is gently withdrawn toward the proximal end of the enteroscope without moving the enteroscope. Then, the overtube balloon is inflated and the enteroscope slowly withdrawn until it reaches the distal end of the overtube.

Technique for retrograde approach

The retrograde approach is a little bit difficult than the oral approach, even for expert endoscopists, with a longer learning curve (20 to 30 cases). It is recommended to

start reduction manoeuvres when looping is first appreciated in the colon. Initial attempts at ileocecal valve intubation should occur with the patient in the left lateral or supine positions in order to achieve an ideal location of the ileocecal valve between the 3 and 9 o'clock positions. In case of failure, it is recommended to change patient position[8].

CLINICAL APPLICATIONS

Single-balloon enteroscopy, such as DBE, allow the possibility of suction and flushing *via* the instrument channel, sampling biopsies, and therapeutic interventions such as argon plasma coagulation, injection, positioning of clips, polypectomy, dilation, and foreign-body extraction, even when inserted distally into the small intestine.

Several study demonstrated its efficacy and safety. Early reports on the use of SBE since its appearance in 2006 involving the prototype XSIF Q160 and its commercially available successor, the SIF Q180, have suggested a high diagnostic yield and similar therapeutic potential to that of the DBE. Ohtsuka and colleagues[9] helped to develop the single-balloon enteroscope in cooperation with Olympus Medical Systems and are credited with the first comparison of single-balloon with double- balloon enteroscopy. They performed 102 procedures in 65 patients with suspected small intestinal disease. Seventy-nine of the procedures were done with the single-balloon enteroscopy system and 11 with double-balloon enteroscopy. Examination time for anterograde insertion was 65.3 min for single-balloon enteroscopy and 74 min for anterograde DBE. Single-balloon enteroscopy retrograde insertion averaged 57.5 min and 56.3 min for retrograde DBE. There were no complications. The investigators concluded it was easy to set up the SBE system and perform the procedure with a single operator. Although not reported, they felt they were able to achieve a high diagnostic yield with the SBE, using their experience with the double-balloon enteroscopy system as a point of reference.

Ramchandani and colleagues[10] studied 60 patients with suspected small bowel disease using the prototype single-balloon enteroscopy system. All patients underwent anterograde examinations; 10 underwent anterograde and retrograde procedures. Mean procedure time was 63 min. The mean depth of insertion was 260 cm beyond the ligament of Treitz. Total enteroscopy was possible in 5 out of 10 cases (50%). Diagnostic yield in cases of obscure gastrointestinal bleeding, chronic abdominal pain, and malabsorption syndrome were 77%, 61%, and 63%, respectively.

Tsujikawa *et al*[4] evaluated 41 patients using the SBE and found it easy to perform, due to the single balloon, and safe to examine the deep small intestine with useful diagnostic and therapeutic capabilities. Other authors with larger series of patients concluded that SBE demonstrated a high diagnostic yield with the real possibility of useful therapeutic interventions[10-13].

Recently, Domagk *et al*[14] published a randomized international multicenter study comparing two balloon-assisted enteroscopy systems: DBE *vs* SBE. A total of 130 patients were included over 12 mo: 65 with DBE and 65 with the SBE technique. Patient and procedure characteristics were comparable between the two groups. Mean oral intubation depth was 253 cm with DBE and 258 cm with SBE, showing non-inferiority of SBE *vs* DBE. Complete visualization of the small bowel was achieved in 18% and 11% of procedures in the DBE and SBE groups, respectively. Mean anal intubation depth was 107 cm in the DBE group and 118 cm in the SBE group. Diagnostic yield and mean pain scores during and after the procedures were similar in the two groups. No adverse events were observed during or after the examinations. This first head-to-head comparison trial of DBE *vs* SBE, comparing the Fujinon DBE system with the Olympus SBE system, demonstrated no difference with respect to the insertion depths. Diagnostic yield, rate of complications between the two systems, and patient discomfort scores during and after the procedures were comparable.

In addition, SBE seems to be a safe procedure. However, scrupulous care is required when passing a small-intestinal lesion or in patients with known adhesions or strictures. Relevant complications, i.e., perforation, in diagnostic balloon-assisted enteroscopy can be expected in approximately 1% of cases. As in conventional endoscopy, the risk is higher in therapeutic enteroscopy, at around 3% to 4%[15].

Among the 622 SBE procedures published to date, only two perforations (0.32%) were occurred: one during diagnostic SBE (in a postoperative case of ulcerative colitis), and one during therapeutic enteroscopy (balloon dilation)[4,13,14,16-19].

In contrast to per oral DBE, no acute pancreatitis has been reported following SBE.

CONCLUSION

SBE is an effective endoscopic tool for the evaluation of the small bowel. Technically, it is easy and safe to perform and it provides similar diagnostic and therapeutic yield when compared with DBE.

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BRIEF ARTICLE

Blue mode does not offer any benefit over white light when calculating Lewis score in small-bowel capsule endoscopy

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Abstract

AIM: To check the usefulness of blue mode (BM) review in lewis score (LS) calculation, by comparing it with respective LS results obtained by white light (WL) small-bowel capsule endoscopy (SBCE) review and mucosal inflammation as reflected by faecal calprotectin (FC) levels, considered as 'gold standard' for this study.

METHODS: Computational analysis of our SBCE database to identify patients who underwent SBCE with PillCam® and had FC measured within a 30-day period from their test. Only patients with prior colonoscopy were included, to exclude any colon pathology-associated FC rise. Each small bowel tertile was reviewed (viewing speed 8 fps) with WL and BM, in a back-to-back mode, by a single experienced reviewer. LS were calculated after each WL and BM reviews. Pearson rank correlation (*rho, r*) statistic was applied.

RESULTS: Twenty-seven (n = 27, 20F/7M) patients were included. Thirteen (n = 13) had SBCE with PillCam®SB1, and the remainder (n = 14) with PillCam® SB2. The median level of FC in this cohort was 125 μg/g. LS (calculated in WL SBCE review) correlation with FC levels was r = 0.490 (P = 0.01), while for BM review and LS correlation with FC was r = 0.472 (P = 0.013).

CONCLUSION: Although BM is believed to enhance mucosal details i.e., small mucosal breaks, it did not perform better than WL in the calculation of LS in our cohort.

Key words: Capsule endoscopy; Lewis score; PillCam; Blue mode; Rapid

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INTRODUCTION

Since its introduction in clinical practice, small-bowel capsule endoscopy (SBCE) has been established as a main, non-invasive imaging modality for the small-bowel. It has already showed to be a superior–to most existing radiological techniques–diagnostic tool in the in-

vestigation of obscure gastrointestinal bleeding (OGIB), although its role in Crohn's (CD) is less clear[1]. Assessment of the full length of the small-intestine is often required not only to evaluate patients with suspected, but also those with established CD[2,3]. However, as the diagnosis of CD remains a clinical one -based on the combination of clinical, radiologic, endoscopic, and histologic findings-, caution is advised in using findings on SBCE as the primary means of making a diagnosis of small-small CD[3]. Furthermore, SBCE is also a useful modality in identifying the impact of non-steroidal anti-inflammatory drugs (NSAIDs), i.e., mucosal breaks, surface denudation and strictures in the small-bowel[4,5].

Until recently, the use of SBCE in monitoring the extent and activity of small-bowel inflammation is limited due to a lack of standardisation in systematically reporting small-bowel mucosal inflammatory change. To this end, Gralnek *et al*[6] developed a scoring index – known since as the Lewis score (LS) - which examines 3 endoscopic parameters: villous oedema, ulceration and luminal stenosis. The investigators set thresholds where LS < 135 denotes normal or clinically insignificant mucosal inflammatory change, LS > 135 and < 790 denotes mild and LS ⩾ 790 severe inflammation.

One of the new features of PillCam® (Given® Imaging Ltd., Yokneam, Israel) reading software (RAPID®) is the integration of the LS and the image enhancement toggle button (in versions 5, 6 and 7). The former provides a screen for LS calculation, while the latter offers both flexible spectral imaging colour enhancement (FICE 1, 2 and 3) as well as blue filtering, all with the simple click of a button. Blue filtering or blue mode (BM) is a colour coefficient shift of light in the short wavelength range (490-430 nm) superimposed onto a white light (WL) (red, blue, green; RGB) image.

Calprotectin, on the other hand, is a protein complex of the S-100 family of calcium binding proteins[7]. It is found in high concentration in the cytosol of neutrophils and is resistant to intestinal degradation for up to a week, thus distributed throughout the stool where it can be readily detected using standard enzyme linked immunosorbent assays (ELISA)[8]. The normal range has been well defined as < 50 μg/g; levels < 20 μg/g are consistent with non-detectable calprotectin in faeces (FC). FC is raised in inflammatory, infective and/or neoplastic enteropathies[9].

Since the initial description by Fagerhol *et al*[10], several studies have been published showing close correlation between faecal calprotectin (FC) concentration and conventional endoscopy, faecal leukocyte excretion quantified with indium, small bowel MRI and SBCE[11-14]. Therefore, FC is considered as a specific and highly sensitive marker of gut inflammation[11,15].

We are set to examine the usefulness of image enhancement, and in particular BM, in calculating the LS, as compared with relevant scores obtained by WL review of SBCE sequences. FC was used as the gold standard for quantifying small-bowel inflammation.

MATERIALS AND METHODS

SBCE video sequences were reviewed with the PillCam® Platform (RAPID®7.0 software), on a 21-inch widescreen monitor using a maximised single view window at a speed of 8 frames per second (fps). The review was performed by a single, experienced reviewer in a room with dimmed lights. Video sequences were not de-identified; however, captured thumbnails were not available to the reader (with the exception of captured anatomical landmarks).

WL review was performed with the Quick Adjust function "on" and with the following predefined settings: sharpness 1, brightness 1 and colour 2.

LS[5] was calculated for each study by inputting the necessary parameters (quantitative and qualitative descriptors relating to villous oedema, ulceration and stenosis) into the RAPID®7.0 workstation algorithm. LS were calculated for each tertile, by switching consecutively between WL and BM review.

In our centre, we have adopted a modified 4-point grading scale (poor, fair, good, and very good; from 0 to 3) to describe small-bowel cleansing. The score depends on the proportion of visualized mucosa and the extent of obscuration by intraluminal food debris, turbid fluids, bubbles or bile as follows: grade 3 (very good visibility): > 75% mucosa visible; grade 2 (good visibility): 50%-75%; grade 1 (average visibility): 25%-50%; and grade 0 (poor visibility): < 25% mucosa seen[16].

Statistical analyses were carried out with a statistical package program for Windows (Minitab® version 16, Minitab Ltd, Coventry, United Kingdom). All *P* values presented herein are 2-tailed. A *P* value < 0.05 was considered statistically significant. Numerical values are herein expressed as median with lower (Q1) and upper (Q3) quartile values following in parentheses. Pearsons' correlation coefficient (*r*, *rho*) was used to measure statistical dependence between two variables.

This study was conducted in accordance with United Kingdom research ethics guidelines. After review by the local ethics committee, further specific ethical review and approval were not required, as the study was considered a retrospective audit work using data obtained as part of regular patient care.

RESULTS

Twenty seven (*n* = 27, 20 females/7 males) patients were included. The median age of the cohort was 40 years (Q1: 24 year, Q3: 55 year). The indications for SBCE were: clinical symptomatology compatible with small-bowel CD (*n* = 19), abnormal small-bowel radiology (*n* = 2), reassessement of established CD (*n* = 3), iron deficiency anaemia ± other clinical symptoms (*n* = 3).

Thirteen (*n* = 13) SBCE were performed with PillCam®SB1, the remaider with PillCam®SB2. The capsule endoscope reached the caecum in 25/27 cases, hence 25 cases were used for further analysis. All 25 patients had undergone, for the purpose of their clinical work-up, a colonoscopy prior (and at a reasonable interval) to their

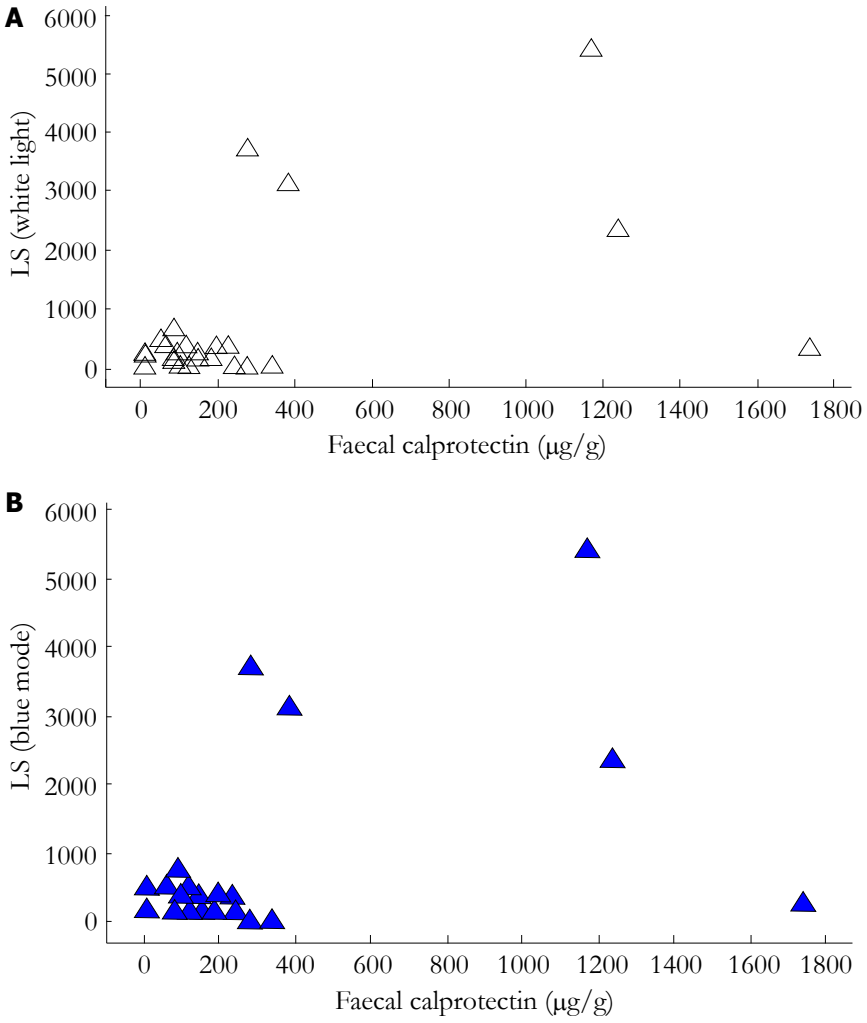

Figure 1 Scatrerplots of correlation between Lewis score calculated with wight light capsule sequence review (A) and with blue mode (B) with faecal calprotectin levels. LS: Lewis score.

SBCE. This was to ensure that the obtained FC results reflected levels of the small-bowel mucosal inflammation and not any colonic pathology[17].

The median small-bowel transit time was 04:11:10, while the median small-bowel cleansing score was assessed at 2.33 (Q1: 1.66, Q3: 2.33). The median FC was 125μg/g (Q1: 87.5 μg/g, Q3: 262.5 μg/g). The median time from obtaining a stool specimen for FC to having SBCE was 0 d (Q1: -6.5 d, Q3: 4.5 d; where the (-) sign denotes that the specimen for FC was obtained after the SBCE was performed).

The correlation between LS (calculated in WL SBCE review) and FC levels was moderate to weak (*rho*: 0.490, $P = 0.010$), while the relevant value for BM SBCE review was *rho*: 0.472, $P = 0.013$. (Figure 1A and B). There was no statistically significant difference between the LS-WL and LS-BM ($P = 0.8976$). When only the ulcer-competent of the LS was examined, BM failed to provide any additional information to WL review ($P = 0.213$).

The cohort ($n = 25$) was then divided further to 3 sub-groups, based on FC results[15]; group A ($n = 8$) with FC < 100 μg/g, group B ($n = 8$) with FC ⩾ 100 μg/g and < 200 μg/g, and group C ($n = 9$) with FC 200 μg/g. In group A, the correlation of LS-WL and LS-BM with FC was *rho* = 0.479 *vs rho* = 0.376 ($P = 0.842$); in group B, *rho* = 0.123 *vs rho* = -0.1653 ($P = 0.845$); and in group C, *rho* = 0.227 *vs rho* = 0.215 ($P = 0.983$), respectively.

Once more, there was no statistical difference between the 2 LS (with WL and BM) calculations in any of the three groups (or groups A, B and C; $P = 0.4388$, 0.3809 and 0.9935, respectively).

DISCUSSION

Lewis Score is considered a standardised means of reporting the presence and degree of clinically significant (irrespective of aetiology) mucosal inflammatory changes seen on CE[2]. It was devised, internally validated and presented in 2006/7, by a group of expert gastroenterologists, from the review of a total of 44 de-identified SBCE studies. Its use helps to reduce subjectiveness, as it is based on the variables/parameters associated with mucosal disease, namely mucosal breaks, villous oedema and stenosis. It has since been incorporated into

the RAPID® software (Given® Imaging Ltd., Yokneam, Israel) and is easily calculated using the parameter entry algorithm.

Image enhancement techniques, such as FICE and BM, have also been incorporated in the RAPID® software. Virtual chromoendoscopy has been already widely used in conventional endoscopy, aiming to improve diagnostic yield by enhancing the contrast between background and surface mucosal abnormalities, through narrowing the bandwidth of WL to that of blue-green light. To date, the published experience of its use in SBCE is only limited[7,18-21]. Furthermore, the ability of chromoendscopy to improve detection rate of clinically significant lesions during SBCE is still questionable[21]. Imagawa *et al*[18] have reported that FICE application provided improved image quality of angioectasias, erosion/ulcerations, and various tumours, when FICE wavelength settings 1 and 2 were used. In a more recent pilot study though[19], the same group found that the detection rate of ulceration/erosion did not differ statistically between conventional i.e., WL-SBCE and FICE-SBCE review.

The experience with BM application in SBCE reading is even more limited[7,1,22]. BM is a colour coefficient shift of light in the short wavelength range (490-430 nm) superimposed onto a WL image. Abdelaal *et al*[22] found that by employing BM in SBCE they detected more superficial erosions and oedema than with WL. They prospectively reviewed a total of 20 SBCE from patients with cirrhosis, at speed of 8 fps, and identified more erosions than with WL. We recently showed that BM provides image improvement for many SBCE lesion categories, but is more useful in enhancing visualisation of surface mucosal changes, e.g., mucosal breaks, ulcerations (in > 90% of cases) and mucosal cobblestoning[7]. This seems to be of particular importance in LS calculation, as one of the three LS parameters is the presence and number of mucosal breaks/ulcers. Although LS has been internally validated, it can be as good as and the current capsule technology level, i.e., lack of directionality, lack of controlled speed of capsule transit, allow to be.

Therefore, in order to compare results from LS calculation with different modes, more objective biochemical markers of small-bowel inflammation i.e. faecal calprotectin or lactoferrin are needed as reference tests. FC is contained in faeces at levels proportional to the amount of neutrophil migration to the intestinal wall and luminal cell shedding. In the absence of colonic pathology, FC levels reflect in an accurate and reliable way, the degree of small-bowel mucosal inflammation[10,12]. As such, it was used as "gold standard" for quantifying small-bowel inflammation, hence mucosal breaks or disruption, for the purposes of this study[23].

With the current study we demonstrated that the use of BM, despite our initial hypothesis[7], offered little aid (in comparison to WL) in LS calculation. In fact, LS calculation with BM showed slighly weaker (as compared to LS-WL) correlation to FC (*rho* = 0.472 *vs rho* = 0.490), although this did not reach statistical significance (P = 0.938). Furthermore, it is worth noting that the correlation between LS (irrespective of viewing mode) and FC was weak (*rho* < 0.5). This could only partially be explained by the fact that the stool specimen collection was obtained on the day of the SBCE test in just one fifth of cases. In the remainder (n = 20), the stool specimen for calprotectin was obtained in period of ± 30 d from the SBCE[12]. Interestingly, Imagawa *et al*[19] also showed that the difference in erosive/ulcerative lesion detection between conventional SBCE and SBCE-FICE (at the various settings) was not statistically significant. This simply means that although chromoendoscopy works well in improving the image quality of captured lesions, it does not lead to improved lesion detection. Of course, this should not come as a surprise, as chromoendoscopy has nothing to do with the various parameters of image acquisition like the speed of small-bowel transit by the capsule, the lack of directionality or the unpredictable change of field of view.

Our study is retrospective and as such it was not possible to standardise the interval between FC measurement and SBCE/colonoscopy. Furthermore, the use of one reviewer following a strict protocol- may have introduced observational bias, when sequentially comparing images in BM and WL.

COMMENTS

Background

The use of small-bowel capsule endoscopy (SBCE) in monitoring the extent and activity of small-bowel inflammation has been limited due to a lack of standardisation in systematically reporting small-bowel mucosal inflammatory change. Lewis score (LS) was developed out of this need and examines 3 endoscopic parameters: villous oedema, ulceration and luminal stenosis. Thresholds are: LS < 135, normal or clinically insignificant mucosal inflammatory change; LS > 135 and < 790, mild inflammation; and LS ⩾ 790 severe inflammation. Furthermore, virtual chromoendoscopy (Fujinon® Intelligent Color Enhancement, FICE) has been incorporated in the Rapid software (Given® Imaging Ltd, Yokneam, Israel) with aim to increase the detection of lesions in capsule endoscopy.

Research frontiers

There are scanty data on the use of virtual chromoendoscopy (FICE or blue mode filter) in small-bowel capsule endoscopy. The crucial question, should this method becomes a regular adjunct in reviewing SBCE videos, is if it improves the detection rate of clinically relevant lesions. Gupta *et al* showed that FICE is not better than white light for diagnosing significant lesions on SBCE for obscure GI bleeding, although some vascular lesions could be more accurately characterized with FICE as compared to white light SBCE. Abdelaal *et al* found that Blue Mode viewing leads to better detection and visualization of vascular and non-vascular lesions. We also extensively checked the use of FICE and Blue Mode in 6 different lesion-categories obtained from 200 capsule endoscopy examinations. We found that comparing with FICE, Blue Mode filter offers better image enhancement in capsule endoscopy.

Innovations and breakthroughs

LS [calculated in white light (WL) SBCE review] correlation with FC levels was r = 0.490 (P = 0.01), while for BM review and LS correlation with FC was r = 0.472 (P = 0.013). There was no statistically significant difference between the LS-WL and LS-BM (P = 0.8976).Although BM is believed to enhance mucosal details i.e., small mucosal breaks, it did not perform better than WL in the calculation of LS in this cohort.

Applications

Data on the validity of virtual chromoendoscopy in SBCE are limited and,

to a great extent, discordant. Further larger scale, multi-center, randomized controlled trial would be of value to determine if has a role in improving diagnosis in SBCE.

Terminology

Virtual chromoendoscopy: an imaging technique that is based on narrowing the bandwidth of the conventional endoscopic image arithmetically, using spectral estimation technology. FICE: (Fuji Intelligent Color Enhancement), Fujinon ® intelligent chromo endoscopy system. Blue filtering or Blue Mode (BM): a colour coefficient shift of light in the short wavelength range (490-430 nm) superimposed onto a WL (red, blue, green; RGB) image. Lewis score (LS): a SBCE inflammation scoring system which examines 3 endoscopic parameters: villous oedema, ulceration and luminal stenosis.

Peer review

The present paper is a retrospective cohort study. The article is well written, and topic is interesting and novel.

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BRIEF ARTICLE

A substantial incidence of silent short segment endoscopically suspected esophageal metaplasia in an adult Japanese primary care practice

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Abstract

AIM: To determine the incidence and characteristics of endoscopically suspected esophageal metaplasia (ESEM) in a primary adult care institution.

METHODS: Eight hundred and thirty two consecutive individuals (mean age, 67.6 years) undergoing upper gastrointestinal endoscopy between January 2009 and December 2010 were included in this study. The diagnosis of ESEM was based on the criteria proposed by the Japan Esophageal Society, and was classified as long segment ESEM (3 cm or more) or short segment ESEM (< 3cm). Short segment ESEM was further divided into circumferential and partial types. Age, gender, hiatus hernia, esophagitis, gastroesophageal reflux disease (GERD)-suggested symptoms, and antacid medications were recorded as background factors. Esophagitis was graded according to the Los Angeles classification. Hiatus hernia was divided into absent and at least partially present.

RESULTS: Long and short segment ESEM were found in 0 and 184 (22.1%) patients, respectively (mean age of short segment ESEM patients, 68.3 years). Male gender and hiatus hernia were shown to be significant factors affecting short segment ESEM by both univariate (P = 0.03 and P = 9.9x10^{-18}) and multivariate [Odds ratio (OR) = 1.45; P = 0.04, and OR = 43.3; P = 1.5x10^{-7})] analyses. Two thirds of patients with short segment ESEM did not have GERD-suggested symptoms. There was no correlation between short segment ESEM and GERD-suggested symptoms.

CONCLUSION: The incidence of short segment ESEM in our community practice seems higher than assumed in Asian countries. As GERD-suggested symptoms are a poor predictor of ESEM, endoscopists should bear in mind that silent short segment ESEM does exist and, in fact, was found in the majority of our patients.

Key words: Endoscopically suspected esophageal metaplasia; Esophagitis; Gastroesophageal reflux disease; Hiatus hernia; Longitudinal vessel

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INTRODUCTION

Barrett's esophagus (BE) is a condition in which the

normal squamous epithelium of the distal esophagus is replaced by specialized intestinal metaplastic epithelium. It is one of the histological consequences of long-standing gastroesophageal reflux disease (GERD)[1] and predisposes to the development of esophageal adenocarcinomas. In Western countries, the incidence of esophageal adenocarcinomas among BE patients was 7/1000-10/1000 person-years duration of follow-up[2], which was thought to constitute a 30 to 120-fold greater risk than that in the general population[3]. An alarmingly rapid increase in esophageal adenocarcinoma has also been reported in some European[4] and Asian countries[5], and, although less marked, in Japan[6]. Accordingly, concern regarding BE as well as GERD has also increased.

Currently, BE is classified into two types according to the length of specialized intestinal metaplasia involved at the lower esophagus: traditional BE or long segment BE (LSBE), with the length being 3cm or more[7]; and short segment BE (SSBE), being less than 3cm[8]. Subsequent follow up examinations[9,10]and a metaanalysis[2] have revealed the development of dysplasia or cancer in SSBE at a substantial rate and an equivalent relative risk ratio of cancer between LSBE and SSBE, suggesting that SSBE *per se* possesses a malignancy potential similar to LSBE. In addition, the length of the columnar epithelium remained unchanged among LSBE patients[11] as well as among many SSBE patients[12], suggesting a fairly rapid evolution of BE to its full length with little subsequent change. Therefore, SSBE should not be overlooked for the early detection of subsequent neoplastic changes arising from it.

In the West, the observed incidence of LSBE and SSBE range from 0.2%-7% and 1%-17%, respectively, in asymptomatic patients[13-16], and from 1%-5% and 1%-19%,respectively, in GERD patients[14-18], while in Central and East Asia, these figures are 0.05%-1.6% and 0.38%-4.6%, respectively, even in patients with reflux symptoms[19-22], suggesting a low incidence of SSBE in Asian countries. In comparison, reports on the incidence of BE in the Japanese population are relatively scant in the literature[12,23-27]. The varying incidence of BE by geographic area might reflect a different awareness and recognition of, or different diagnostic criteria[27-30] for, this entity as well as a different and biased study population such as veterans[13], those undergoing colon cancer screening[15,16], or those seen at a gastroenterological tertiary center[14,21,22]. Therefore, the aim of this study is to elucidate the incidence and characteristics of this condition in the less selective, less biased study cohort of daily general practice. Since the Japan Esophageal Society proposed endoscopically diagnosed esophageal metaplasia (ESEM) as an endoscopic diagnosis of BE and no requirement of histological evidence[30,31], we adopted the ESEM criteria proposed by the Japan Esophageal Society and investigated consecutive adult primary care patients irrespective of reflux symptoms, including practically asymptomatic individuals undergoing an annual health check examination. Thus, our study population resembled that seen by the general practitioner.

MATERIALS AND METHODS

The study population consisted of consecutive patients who underwent a referral (n = 400) or screening (n = 432) upper gastrointestinal endoscopy for a variety of clinical reasons or as a part of their annual medical examination in our Unit between January 2009 and December 2010. Our Unit is independent of gastroenterological tertiary centers and the patients were residents in the neighboring district to our institution with easy access to us. The clinical indications of referral endoscopy included GERD symptoms (n = 305) listed in the published questionnaires[32-35] (heartburn, regurgitation, dysphagia, odynophagia, epigastralgia, belching, nausea and vomiting, and non-cardiac chest pain) or other gastrointestinal symptoms such as abdominal pain (n = 6), or loss of appetite with or without a clinically important weight loss (n = 48). Other conditions unrelated to gastrointestinal symptoms but accepted indications for endoscopy included abnormalities of laboratory findings (n = 29), positive fecal occult blood test (n = 10), and other miscellaneous factors (n = 2). Histamine 2 receptor antagonists or proton pump inhibitors were regarded as antacid medications. The symptoms and antacid medications at the time when submitted for the first endoscopy were recorded. The patients who underwent therapeutic or urgent endoscopies, or who had undergone previous gastric or esophageal surgery including antireflux surgery were excluded, while those having undergone previous endoscopic mucosal resection were permitted. For patients undergoing multiple endoscopies during this study period, only the endoscopic data attained during the first endoscopy were used in this study.

The definition of ESEM was based on the anatomical criteria proposed by the Japan Esophageal Society[30,31]. Before the fiberscope was inserted into the stomach, the squamocolumnar junction (SCJ), diaphragmatic hiatus, and, if present, longitudinal vessels at the lower esophagus were recognized with only minimal air inflation. The SCJ was recognized as a distinct difference in color between a reddish-orange velvety gastric epithelium and a whitish-gray smooth esophageal epithelium. The diaphragmatic hiatus appeared endoscopically as a narrowing or notch of the lower end of the esophagus where the tubular esophagus flared to become the sack-like stomach. The gastroesophageal junction (GEJ) was defined at the distal margin of the longitudinal vessels; thus, the columnar epithelium on the longitudinal vessels, if present, was diagnosed as ESEM and was further categorized according to its length: long segment ESEM when circumferentially recognized with a minimal length of 3cm or more, or short segment ESEM for length less than 3 cm[27]. In the cases of severe esophagitis, which hindered correct recognition of longitudinal vessels, the GEJ was defined at the proximal margin of the gastric fold[36]. These measurements were recorded using the

Table 1 Demographic and endoscopic characteristics of 832 patients with or without short segment ESEM

		Total (%) (n = 832)	Short segment ESEM(+) (%) (n = 184)	ESEM(-) (%) (n = 648)	P value
Age (yr), mean ± SD		67.6 ± 12.9	68.3 ± 12.2	67.4 ± 13.0	0.41
Age (yr), decennium	80-	139 (16.7)	31 (16.8)	108 (16.7)	0.92
	70-79	266 (32.0)	63 (34.2)	203 (31.3)	
	60-69	249 (29.9)	51 (27.7)	198 (30.6)	
	50-59	97 (11.7)	21 (11.4)	76 (11.7)	
	40-49	52 (6.2)	13 (7.2)	39 (6.0)	
	-39	29 (3.5)	5 (2.7)	24 (3.7)	
Age (yr), dichotomy	70-	405 (48.7)	94 (51.1)	311 (48.0)	0.46
	-69	427 (51.3)	90 (48.9)	337 (52.0)	
Gender	Male	339 (40.7)	88 (47.8)	251 (38.7)	0.03
	Female	493 (59.3)	96 (52.2)	397 (61.3)	
Antacid therapy	(+)	196 (23.6)	52 (28.3)	144 (22.2)	0.09
	(-)	636 (76.4)	132 (71.7)	504 (77.8)	
GERD-suggested symptoms	(+)	305 (36.7)	68 (37.0)	237 (36.6)	0.92
	(-)	527 (63.3)	116 (63.0)	411 (63.4)	
Esophagitis	(+)	45 (5.4)	10 (5.4)	35 (5.4)	0.73
	(-)	787 (94.6)	174 (94.6)	613 (94.6)	
Hiatus hernia	(+)	621 (74.6)	182 (98.9)	439 (67.7)	9.9×10^{-18}
	(-)	211 (25.4)	2 (1.1)	209 (32.3)	

ESEM: Endoscopically suspected esophageal metaplasia; GERD: Gastroesophageal reflux disease.

markings of the endoscopic shaft. The shapes of the short segment ESEM were categorized as circumferential or partial types. The hiatus hernia was determined by subtracting the area of ESEM from the area between the SCJ and diaphragmatic hiatus, and then divided into absent or at least partially present. Reflux esophagitis was endoscopically scored as grade A, B, C, or D according to the Los Angeles classification[37].

For univariate analysis, Fisher's exact tests were used to compare categorical data. An unpaired Student t test was used for the comparison of two mean values. For multivariate analysis, a logistic regression method was employed to investigate the factors affecting the presence of short segment ESEM. P values of less than 0.05 were considered significant.

This study followed the principles of the declaration of Helsinki.

RESULTS

This study comprised 832 patients (mean age 67.6 years old, 40.7% male). Long and short segment ESEM wereidentified in 0 and 184 (22.1%) patients,respectively. Thus, the subsequent analyses focused on short segment ESEM (n = 184) and non ESEM patients (n = 648).

Overall, 405 (48.7%) patients were aged 70 years or older, while 81 (9.7%) patients were < 50 years old (Table 1). Univariate analysis showed that short segment ESEM was correlated with male gender (P = 0.03) and hiatus hernia (P = 9.9 $\times 10^{-18}$) (Table 1). Surprisingly, GERD-suggested symptoms were negative in 63% of short segment ESEM patients and did not correlate with short segment ESEM, indicating that approximately two thirds of short segment ESEM patients were silent. Patients with (n = 305) or without (n = 527) GERD-suggested symptoms exhibited almost the same incidence of short segment ESEM (22.3% and 22.0%, respectively). Logistic regression analysis also showed that male gender (P = 0.04) and hiatus hernia (P = 1.5 $\times 10^{-7}$) were significant factors affecting short segment ESEM (Table 2). Again, GERD-suggested symptoms did not correlate with short segment ESEM. Among the 184 patients with short segment ESEM, a partial type was observed in 129 (70.1%) patients. The types of short segment ESEM did not correlate with any of the background factors.

Grades A, B, C, and D esophagitis were observed in 17, 19, 3, and 6 patients, respectively. Neither endoscopically suspected dysplasia nor adenocarcinoma arising from the ESEM that required biopsy was documented.

DISCUSSION

The merit of our study is its application to consecutive individuals in a community practice irrespective of GERD-suggested symptoms. In sharp contrast to the reported incidence of LSBE (0.05%-1.6%), or SSBE (0.4%-4.6%), or even endoscopically diagnosed BE (ESEM) (1.5%-10%) in Asian countries[19-22], we have demonstrated that long and short segment ESEM were observed in 0% and 22.1%,respectively, of the study population, rates in accordance with (0.2%-0.5% and 20%-43%)[12,25-27] or even higher than (0.2%-0.6% and 12.0%-15.1%)[23,24] those reported from Japan. Our results suggest that the incidence of short segment ESEM is greater than assumed in Asian countries irrespective of tertiary or primary care institutions.These differences among geographic areas might reflect different levels of awareness and recognition of this entity, diagnostic criteria (biopsy proven or endoscopically), or a different study population (GERD patients or asymptomatic individuals). In addition, age of the study population may account for the differences. As compared with the incidence of short segment ESEM in the present study, a lower or similar incidence of SSBE was respectively reported in a cohort with a mean age younger than (47-61 years old)[13-15,20-24] or similar to (66-69 years old)[12,26] those in our study population. Further more, a substantially high incidence of short segment ESEM in the present study may only be an approximation of the real incidence due to the easily accessible gastrointestinal unit. Since no universally accepted definition of BE currently exists[27-30], the diagnostic criteria for this condition in the West and in Japan should be first compared and discussed.

In the West, the diagnosis of LSBE and SSBE is

Table 2 Logistic regression analysis of association between short segment ESEM and background factors

		Odds ratio	95% Confidence interval	*P* value
Age		1.01	0.99-1.02	0.28
Gender	Female	1	-	
	Male	1.45	1.02-2.06	0.04
Antacid therapy	(-)	1	-	
	(+)	1.23	0.83-1.84	0.3
GERD-suggested symptoms	(-)	1	-	
	(+)	1.08	0.75-1.57	0.67
Esophagitis	(-)	1	-	
	(+)	0.74	0.35-1.58	0.44
Hiatus hernia	(-)	1	-	
	(+)	43.3	10.6-176.1	1.5×10^{-7}

GERD: Gastroesophageal reflux disease; ESEM: Endoscopically suspected esophageal metaplasia.

based on multiple, systematic, and targeted biopsies confirming specialized intestinal metaplasia[28] or a columnar-lined epithelium[29]. In order to determine the optimal site of biopsy, precise recognition of the GEJ is a prerequisite; however, current difficulties include a lack of endoscopic landmarks for the GEJ. Although the GEJ is defined as the proximal margin of the gastric folds in the West, its appearance changes from moment to moment under live endoscopy, depending on inspiration, peristaltic activity, and gagging reflux with a transient prolapse of gastric folds up into the esophagus. In addition, gastric mucosal atrophy and air overinflation with the subsequent disappearance of gastric folds hamper identification of the "true" proximal margin of the fold. Furthermore, intestinal metaplasia can exist at the SCJ even in individuals without BE[38], suggesting a false positive diagnosis of BE. On the other hand, failure to detect intestinal metaplasia in 20% or more of BE patients[39,40] suggests a false negative diagnosis of BE.

It is widely accepted in Japan that the distal margin of the palisade-shaped longitudinal capillary vessels corresponds to the GEJ. Therefore, longitudinal vessels emanating from the SCJ, if they locate in the area of reddish-orange velvety mucosa distally to the SCJ, can be considered ESEM, and histological evidence of goblet cells is not mandatory[30,31]. The rationale for these criteria is supported by several anatomical and molecular biological findings. The longitudinal vessels are specifically located in the lamina propria of the esophagus[41]. Analyses of protein[42] or gene[43] expression have provided phenotypic evidence of intestinal differentiation in the endoscopically defined SSBE or in the metaplastic but nongoblet esophageal columnar lined epithelium. Patients with a columnar-lined epithelium with or without specialized intestinal metaplasia carry a similar risk of developing esophageal adenocarcinoma[44]. Furthermore, the Japanese criteria have merit due to the endoscopic diagnosis accompanied by atraumatic procedures with lower cost and ease, readily allowing general practitioners to adopt this technique and thus facilitating the endoscopic description of BE, especially for those with conditions liable to bleeding such as liver cirrhosis, coagulopathies, or anticoagulant therapies. Indeed, Western experts have also emphasized the value of the Japanese criteria[45] and Western endoscopists have actually been able to recognize the distal margin of the longitudinal vessels similar to Japanese endoscopists[46].

In the present study, 36.7% of patients showed GERD-suggested symptoms. This incidence seems to be higher than those reported from Asia (2.5%-4.8%) and the West (16%-28%)[47]. However, such a comparison requires caution because the incidence of GERD is influenced by many factors including disease awareness as well as diagnostic criteria such as symptomatology and its frequency threshold. In the present study, we did not use precise questionnaires and did not consider symptom frequency for the consideration of GERD because, in consideration of ESEM and efforts toward its detection, we believe that GERD or other gastrointestinal symptoms *per se* by which the patients are willing to undergo endoscopy are more important for the initiation of endoscopy. It is noteworthy that, when symptom frequency was not taken into account, the incidence of GERD was higher both in Japan (15.8%-44.1%)[48-50] and in Asian countries (32.3%-41.2%)[51-53], which is consistent with the findings in the present study.

Despite the higher incidence of GERD-suggested symptoms, short segment ESEM did not correlate with GERD-suggested symptoms or esophagitis. Importantly, 63% of the short segment ESEM patients in our series did not have typical reflux symptoms, suggesting the existence of silent ESEM. It is unlikely that the antacid therapy was attributable to silent ESEM because multivariate analysis found neither GERD-suggested symptoms nor antacid therapy to be significant factors for short segment ESEM. These findings are in accordance with previous studies[14,21] and a recent metaanalysis[54] which demonstrated no association between SSBE and GERD. On the other hand, we observed that short segment ESEM was strongly correlated with hiatus hernia. The higher incidence (75%) of hiatus hernia in the present study compared with those (18%-30%) in previous studies[55,56] may be ascribed partly to the different definition and classification of hiatus hernia and partly to the different age distributions. Even the presence of partial hiatus hernia was included in our study, while a hiatus hernia of only 2 cm or more was considered in most studies[56-58]. Patients aged 70 years or more comprised 49% of our study, while this figure in other studies was 27%[55,56]. Indeed, other investigators also observed that hiatus hernia was positively correlated with older age[55] and BE[57]. The inclusion criteria for hiatus hernia in the present study may have accounted for most (99%) short segment ESEM patients having hiatus hernia, which resulted in the wide range in the 95% confidence interval of the odds ratio. Although different definitions and

classifications of hiatus hernia employed by each study group undoubtedly influence the strength of the association between hiatus hernia and short segment ESEM, and hamper comparisons between publications reporting such associations, it is assumed that a hiatus hernia is likely to cause acid reflux, at least asymptomatically, and ESEM could eventually develop. Therefore, patients with short segment ESEM have backgrounds liable to cause acid reflux such as a hiatus hernia, while the majority of short segment ESEM patients are unaware that they have the condition, thus may not be diagnosed unless endoscopy is performed.

These considerations might explain our findings of no correlation between age and the incidence of short segment ESEM. In fact, there seems inconsistency in the literature concerning the correlation between older age and incidence of BE, which was positive in some reports[11,12] and neutral in another[27], the latter findings being in agreement with those of the present study. A higher incidence of hiatus hernia in the present study reflects the likely establishment of short segment ESEM regardless of age, which could provide one plausible explanation for such a neutral correlation.

The recognition of silent short segment ESEM remains a problem. Considering the paradigm that BE arises as a complication of GERD and predisposes to esophageal adenocarcinomas, asymptomatic short segment ESEM highlights the need to assess the distal esophagus carefully in all patients undergoing upper endoscopy for any indication.In this study population which had easy access to our gastrointestinal unit, our results demonstrate that short segment ESEM exists at a substantial rate even in asymptomatic patients, but can not be predicted by symptoms, a fact endoscopists should bear in mind.

COMMENTS

Background

The incidence of Barrett esophagus (BE) varies in the literature, depending on different awareness and recognition of, or different diagnostic criteria for, this entity as well as different biased study populations. Reports on the incidence of BE in the Japanese population are scantin the literature.

Research frontiers

It has been proposed that BE, even in its short segment, should not be overlooked for the early detection of subsequent neoplastic changes arising from it. The aim of this research was to clarify the incidence and characteristics of BE in the less selective, less biased study cohort of daily general practice, thus the study population resembled that seen by the general practitioner. For this purpose, the authors applied endoscopically suspected esophageal metaplasia (ESEM) as an endoscopic diagnosis of BE. The merits of the criteria used were an endoscopic diagnosis accompanied by atraumatic procedures and no requirement of histological findings, with lower cost and ease, resulting in general practitioners adopting this technique and thus facilitating the endoscopic description of BE.

Innovations and breakthroughs

The incidence of short segment ESEM in the authors' series seems higher than those reported in Asian countries. The symptoms that suggest gastroesophageal reflux disease (GERD) are a poor predictor of ESEM, suggesting that a substantial number of patients have silent short segment ESEM, a fact endoscopists should bear in mind.

Applications

Asymptomatic short segment ESEM highlights the need to carefully assess the distal esophagus in all patients undergoing upper endoscopy for any indication. This will result in the likelihood of detecting esophageal adenocarcinomas at an earlier stage since BE predisposes to esophageal adenocarcinomas.

Terminology

The definition of ESEM was based on the anatomical criteria proposed by the Japan Esophageal Society. The columnar epithelium on the longitudinal vessels emanating from the squamocolumnar junction was diagnosed as ESEM. ESEM was further categorized according to its length: long segment ESEM when circumferentially recognized with a minimal length of 3cm or more, or short segment ESEM for length less than 3 cm.

Peer review

Although this paper is a simple observational study from a single center looking at endoscopic diagnosis of esophageal metaplasia in a Japanese cohort, study population at primary adult care institution is attractive and the important findings are the presence of ESEM not related to symptoms.

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BRIEF ARTICLE

Effectiveness of outpatient percutaneous endoscopic gastrostomy replacement using esophagogastroduodenoscopy and propofol sedation

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Abstract

AIM: To evaluate the effectiveness of outpatient percutaneous endoscopic gastrostomy (PEG) replacement using esophagogastroduodenoscopy (EGD) and propofol sedation.

METHODS: We retrospectively assessed the outcome and complications of consecutive patients referred for PEG replacement which was performed using EGD under propofol sedation in the outpatient setting. The success rate, the mean dose of propofol, procedure time, EGD findings, discharge time from endoscopy unit, respiratory depression, and complications within 72 h of the procedure were evaluated. In a subset of these patients, the blood concentrations of propofol were measured.

RESULTS: All 221 patients underwent successful PEG replacement. The mean dose of propofol was 34 mg (range, 20-60 mg) with a mean procedure time of 5.9 min (range, 3-8 min). Reflux esophagitis (12 patients), gastric ulcer (5), gastric neoplasm (2), and duodenal ulcer (1) were newly diagnosed at replacement. Discharge from endoscopy unit was possible in 100% of patients 45 min after the procedure. Only 3.6% (8) required transient supplemental oxygen. No complications occurred within 72 h of the procedure. During EGD the level of sedation and propofol blood concentrations after administration of propofol (30 mg) in these PEG patients corresponded to those of propofol (60 mg) in middle aged subjects (control).

CONCLUSION: PEG replacement using EGD and propofol sedationin the outpatient setting was safe and practical.

Key words: Esophagogastroduodenoscopy; Gastrostomy; PEG; Propofol

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INTRODUCTION

The number of patients receiving percutaneous endoscopic gastrostomy (PEG) placement has dramatically increased[1,2]. The two commonly used methods of PEG replacement in Japan are replacement using esophagogastroduodenoscopy (EGD) or fluoroscopy in the outpatient setting in a hospital and replacement without EGD or fluoroscopy at the patient's home or nursing home. PEG replacement in the hospital is thought to be safer, but is more expensive than that at the patient's home or nursing home. Propofol is a good sedative agent for endoscopic procedures, in that it is superior to benzodiazepines with regard to rapidity of induction of sedation and is associated with a faster recovery[3-6]. Propofol sedation in high risk and elderly patients undergoing endoscopic procedures has been reported to be both safe and effective[7-15]. The aim of this study was to evaluate the effectiveness of PEG replacement using EGD and low-dose propofol sedation in the outpatient setting.

MATERIALS AND METHODS

Patients

PEG procedures were performed in 251 patients between January 2008 and December 2010 at Showa Inan General Hospital. We retrospectively enrolled patients who underwent PEG replacement at our hospital over a three-year period. Inclusion criteria included patients whose catheters were clogged and whose catheters had not been replaced in the previous 4 mo. Exclusion criteria included patients who received prior gastric surgery (21 patients) and those who were assigned to American Society of Anesthesiologists (ASA) class IV (9 patients) as well as those allergic to the drugs used or its components (soybean or egg).The endoscopic team consisted of a nurse administering the drugs and responsible for the patient, the endoscopist, the physician who performed PEG replacement and a second nurse to assist the endoscopist and the other nurse. Both the nurses and physicians had advanced cardiac life support certification. Written informed consent for PEG replacement was obtained before PEG replacement. For patients unable to give consent, consent was obtained from family members. This retrospective study was approved by the ethics committee at Showa Inan General Hospital.

PEG replacement using this method

PEG replacement was performed using a bumper-tube-type catheter (Ponsky NBR catheter, Medicon, Osaka, Japan) or a bumper-button-type catheter (Ideal Button, Olympus, Tokyo, Japan). The catheter used was chosen according to patients or their family members' requests. Under propofol sedation, conventional EGD was performed in the supine position using the standard endoscope and then PEG replacement was performed endoscopically.

Propofol sedation

As we previously reported[6,15], a butterfly needle for the bolus injection of propofol was placed in the patient's forearm shortly before the start of EGD and removed after completion of the procedure. Propofol (Diprivan, Astra Zeneca, Japan) was given by bolus injection with a standard protocol of 40 mg for patients < 70 years old, 30 mg for patients aged 70 to 89 years, and 20 mg for those 90 years or older. Adequate sedation was achieved when the patient passed through the following sequence: eyes closing, one or two yawns, and cessation of body movements. The target level of sedation was moderate conscious sedation with the patient still able to respond purposefully to verbal commands. When the target level was not obtained or the patients were undersedated, an additional injection of 10-20 mg of propofol was given.

When the peripheral oxygen saturation (SpO_2) was less than 90%, a standard chin lift maneuver was promptly performed by the nurse. If oxygen desaturation continued for more than 20 s, supplemental oxygen was given. Vital signs were frequently assessed. In addition to the monitoring of vital signs, the patients' condition was also assessed more globally by visual inspection. Monitoring and complications were recorded by a registered nurse. SpO_2 was routinely captured by visual inspection of the monitor and the value was recorded on the vital sign sheet.

After the procedure,patients were moved to the waiting room and were discharged after they were awake. The patient's conscious condition was assessed every 15 min starting 30 min after the procedure. The nurses reconfirmed the absence of reemerging sedative effects and finally permitted patients to leave the endoscopic unit.

Study design

The success rate, procedure time, EGD findings, discharge time from endoscopy unit and complications within 72 h after the procedure were retrospectively evaluated. The complications were defined as aspiration pneumonia, bleeding, perforation and peritonitis. During a 3-day period after the procedure, patients' conditions were followed up and recorded using information from health care providers. The patients returned to our hospital if problems occurred or to change the catheter. It was recommended to the families that the catheter be changed about six months after the initial PEG placement to prevent catheter deterioration. The actual decision to replace a catheter was made based on signs of tube blockage confirmed by health care providers. Tube blockage was defined as loss of patency for nutrient flow through the PEG lumen. Exchange systems consisted of the ideal button or the Ponsky gastrostomy catheter depending on the wishes of the caregiver.

Other parameters recorded during chart review included demographic data (i.e., age, sex, indications for the procedure, time to replacement, number of replacements and type of PEG catheter used).

Table 1 Demographic and baseline characteristics of 221 patients

Gender (male/female)	127/94
Age (yr) (mean ± SD)	81 ± 14
Indication for PEG	
CVA/CNSD/tumor	136/77/8
Number of replacement	
1	127 (57%)
2	58 (26%)
3 and more	36 (16%)
Time to replacement (d) (mean ± SD)	271 ± 53
Type of catheter used previously	
Bumper-tube-type	106
Bumper-button-type	103
Balloon-tube-type	4
Balloon-button-type	8

Values are numbers of patients except for age and time to replacement. PEG: Percutaneous endoscopic gastrostomy; CVA: Cerebrovascular accident; CNSD: Central nervous system disorders.

Blood concentrations of propofol

Blood levels of propofol were measured before and 30, 60 and 120 min after the completion of drug administration. The measurement of propofolblood concentration was performed according to previously described methods[16]. For the measurement of propofol, acetnitrile and internal standardwere added to a plasma sample and vortexed for 1 min. Following centrifugation at 13 000 rpm for 5 min, 50 μL aliquots of the supernatant were directly injected into the HPLC systemconsisting of a C18 reversed-phase column. Propofol and the internal standard (thymol) were quantified using coulometric electrochemical detection.

Statistical analysis

Data are presented as means and standard deviations. The Chi-square test, with Yates' correction for continuity where appropriate, was used for comparison of categorical data. Fisher's exact test was used when the numbers were small. For parametric data, the Student's *t* -test was used when 2 means were compared. A value of $P < 0.05$ was regarded as significant. All statistical evaluations were performed using SPSS version 12.0 J software (SPSS Japan Inc., Tokyo, Japan).

RESULTS

Two hundred and twenty-onepatients were enrolled in this retrospective study. The demographic and baseline characteristics of these patients are shown in Table 1. All were elderly with a mean age of 81 years. In 57% of patients this was the first PEG replacement. A bumper-type catheter was present in 95% (209/221) of patients and the time to replacement averaged 271 ± 53 d. As shown in Table 2, all PEG replacements were successful. The mean dose of propofol administered was 34 mg (range, 20-60 mg). Mean procedure time was 5.9 min (range, 3-8 min). As a result of conventional EGD before and after replacement, reflux esophagitis (12 patients), gastric ulcer (5), gastric neoplasm (2), and duodenal ulcer (1) were newly diagnosed. Discharge from the endoscopy unit was possible in 100% of patients 45 min after the procedure. Eight patients (3.6%) required transient supplemental oxygen; neither mask ventilation nor endotracheal intubation was required. No complications occurred within 72 h of the procedure (Table 2).

Table 2 Outcomes and complications of this percutaneous endoscopic gastrostomy replacement method

Successful procedure	221 (100%)
Propofol dose (mg) (mean ± SD)(range)	34 ± 11 (20-60)
Mean procedure time (range)(min)	5.9 (3-8)
EGD findings newly recognized (%)	
Reflux esophagitis	12 (5.4)
Gastric ulcer	5 (2.3)
Gastric neoplasm	2 (0.9)
Duodenal ulcer	1 (0.5)
Type of new catheters chosen	
Bumper-tube-type	112
Bumper-button-type	109
Oxygen administered	8 (3.6%)
Mask ventilation required	0
Heart rate < 50 beats/min	0
Blood pressure < 70 mmHg	0
Discharge within 45 min after the procedure	221 (100%)
Complications within 72 h of the procedure	
Aspiration pneumonia	0
Bleeding	0
Perforation	0
Peritonitis	0

Values are numbers of patients except for procedure time and propofol dose. EGD: Esophagogastroduodenoscopy.

When propofol was administered to these patients undergoing outpatient PEG replacement, blood concentrations of propofol dramatically decreased from 130 ± 36 ng/mL at 30 min to 37 ± 11 ng/mL at 120 min. Although the total dose of propofol used in these patients was only 50% of the total dose used in middle aged patients (30 mg *vs* 60 mg), similar sedation level and propofol blood concentrations were obtained (Table 3).

DISCUSSION

Although PEG replacement is generally considered safe, the procedure can be associated with complications[17,18]. In Japan, PEG replacement is often performed in the patient's home or nursing home without EGDor fluoroscopy. Non-endoscopic methods to determine correct catheter placement include insufflation of air, indigocarmine solutions, or ultrasound[19-21]. Suzuki *et al*[20] reported that PEG catheter misplacement was detected at a frequency of 0.4% in 961 patients using indigocarmine solution. Therefore, PEG replacement using EGD would improve the safety of PEG replacement, independent of the technical difficulty.

Although the dose of propofol required for endoscopy sedation is thought to be correlated to body

Table 3 Comparison of blood concentrations of propofol between PEG replacement patients and middle aged subjects who underwent esophagogastroduodenoscopy

	PEG replacement (n = 20)	Middle age (n = 20)	P value
Gender (M/F)	10/10	10/10	
Age (yr)	78 ± 2	52 ± 6	< 0.0001
Body weight (kg)	54 ± 9	57 ± 6	0.41
Dose used (mg)	30	60	
Sedation level (moderate)	20	20	
Blood propofol concentrations (ng/mL)			
30 min after injection	130 ± 36	125 ± 35	0.55
60 min	60 ± 22	55 ± 19	0.47
120 min	37 ± 11	29 ± 14	0.45

Values are mean ± SD except for gender and sedation level (numbers of patients). PEG: Percutaneous endoscopic gastrostomy.

weight, our previous study demonstrated that low-dose sedation (20-40 mg) for elderly patients was sufficient to provide adequate sedation and patient comfort[6,15]. The protocol adopted in our study was strongly focused on safety, and the initial dose of 20-40 mg of propofol was designed to minimize hypoxemia during PEG replacement. In this study, low-dose of propofol was associated with a low frequency of respiratory depression except for critically ill patients (ASA class Ⅳ). Therefore, even in elderly and class ASA Ⅲ patents undergoing PEG placement, the use of propofolallows fast recovery and may contribute to the low risk of respiratory depression or aspiration.

In Japan, benzodiazepines are widely used for sedation during EGD. However, the action of these drugs continues for a long time and prolonged monitoring may be necessary to ensure recovery before allowing the patient to return home. As complications including aspiration pneumonia did not develop within 72 h of the procedure (Table 2), this study showed that PEG replacement using propofol sedation was safe even in the outpatient setting. From these results, we suggest that propofol should be used as the drug of choice for endoscopic PEG replacement in the outpatient setting.

In this study, the dosage of propofol used averaged 34 mg (0.6 mg/kg). This dose was only 50% of the total dose used in middle aged patients and enabled these PEG patients to obtain a similar sedation level and propofol blood concentrations (Table 3), resulting in early discharge from the endoscopy unit after the procedure. One additional advantage of EGD before or after replacement is that it identified new and potentially treatable problems in 20 patients (9%) (Table 2). Therefore, EGD under low-dose propofol sedation may improve acceptability and quality of PEG replacement in the outpatient setting.

When the bumper-type catheter was used, the mean time to replacement was approximately 9 mo and the annual cost would be approximately 525 US dollars /patient with an average of approximately 1.5 replacements per year (Table 1). Therefore, even if the charge required to transport the patient to and from the hospital was added, the annual cost using this method would be less than that of replacement at the patient's home or nursing home which requires more frequent replacements of the balloon-type catheter.

The present study has some limitations in relation to the dose and cost of propofolduring the procedure. Usually, the dose of propofol as well as other sedatives used for endoscopy is adjusted according to the age and weight of the subject. However, in this study, the dose was adjusted only according to the age of the subject. For elderly PEG patients,weight was not considered important for adjusting the dose of propofol. One of the reasons for this may be that the procedure time was very short (average, 5.9 min).

In addition, although the manufacturer recommends that the balloon type of PEG cathetershould be replaced once per month,this is frequently not followed, balloon type catheters generally need to be changed more frequently than bumper type catheters. On the other hand, the bumper type of PEG catheter requires to be changed one or two times per year, and without EGD or fluoroscopy the catheter may be misplaced. Although the procedure identified new treatable problems in some patients and was safely performed in the outpatient setting in this study, four items were needed to perform our procedure. Therefore, the total cost related to the procedure would increase even if the cost was much lower than that of the procedure which required hospitalization.

In conclusion, EGD using low-dose propofol sedation allowed safe and practical PEG replacement in the outpatient setting.

COMMENTS

Background

The number of patients receiving percutaneous endoscopic gastrostomy (PEG) placement has dramatically increased. The two commonly used methods of PEG replacement in Japan are replacement using esophagogastroduodenoscopy (EGD) or fluoroscopy in the outpatient setting in a hospital and replacement without using EGD or fluoroscopy at the patient's home or nursing home. PEG replacement in the hospital is thought to be safer, but is more expensive than that at the patient's home or nursing home.

Propofol is a good sedative agent for endoscopic procedures as it is superior to benzodiazepines with regard to rapidity of induction of sedation and is associated with a faster recovery. Propofol sedation in high risk and elderly patients undergoing endoscopic procedures has been reported to be both safe and effective.

Research frontiers

This study reported on the effectiveness of PEG replacement using EGD and low-dose propofol sedation in the outpatient setting.

Innovations and breakthroughs

In this study,all patients underwent successful PEG replacement. The mean dose of propofol was 34 mg (range, 20-60 mg) with a mean procedure time of 5.9 min (range, 3-8 min). Reflux esophagitis, gastric ulcer, gastric neoplasm, and duodenal ulcer were newly diagnosed at replacement. Discharge from the endoscopy unit was possible in 100% of patients 45 min after the procedure. No complications occurred within 72 h of the procedure. During EGD, the level of sedation and propofol blood concentrations after administration of propofol

(30mg) in these PEG patients corresponded to those of propofol (60 mg) in middle aged subjects (control). In conclusion,PEG replacement using EGD and propofol sedationin the outpatient setting was safe and practical.

Applications

PEG replacement using EGD and propofol sedationin the outpatient setting would be promising worldwide.

Peer review

The present paper is a retrospective study. The article is well written.

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Events Calendar 2012

January 19-21, 2012
American Society of Clinical Oncology 2012 Gastrointestinal Cancers Symposium
San Francisco, CA 3000, United States

January 19-21, 2012
2012 Gastrointestinal Cancers Symposium
San Francisco, CA 94103, United States

January 20-21, 2012
American Gastroenterological Association Clinical Congress of Gastroenterology and Hepatology
Miami Beach, FL 33141, United States

February 2-4, 2012
14th Dusseldorf International Endoscopy Symposium 2012
Dusseldorf, Germany

February 24-27, 2012
Canadian Digestive Diseases Week 2012
Montreal, Canada

March 1-3, 2012
International Conference on Nutrition and Growth 2012
Paris, France

March 7-10, 2012
Society of American Gastrointestinal and Endoscopic Surgeons Annual Meeting
San Diego, CA 92121, United States

March 12-14, 2012
World Congress on Gastroenterology and Urology
Omaha, NE 68197, United States

March 30-April 2, 2012
Mayo Clinic Gastroenterology and Hepatology
San Antonio, TX 78249, United States

March 31-April 1, 2012
5th Annual Endoscopy Directors Meeting Endoscopy Unit Management in the 21st Century: Issues, Solutions, and Plans for the Future
Washington, DC 20057, United States

April 8-10, 2012
9th International Symposium on Functional GI Disorders
Milwaukee, WI 53202, United States

April 15-17, 2012
European Multidisciplinary Colorectal Cancer Congress 2012
Prague, Czech

April 19-21, 2012
Internal Medicine 2012
New Orleans, LA 70166, United States

April 20-22, 2012
Diffuse Small Bowel and Liver Diseases
Melbourne, Australia

April 22-24, 2012
EUROSON 2012 EFSUMB Annual Meeting
Madrid, Spain

April 28, 2012
Issues in Pediatric Oncology
Kiev, Ukraine

May 3-5, 2012
9th Congress of The Jordanian Society of Gastroenterology
Amman, Jordan

May 7-10, 2012
Digestive Diseases Week
Chicago, IL 60601, United States

May 17-21, 2012
2012 ASCRS Annual Meeting-American Society of Colon and Rectal Surgeons
Hollywood, FL 1300, United States

May 18-23, 2012
SGNA: Society of Gastroenterology Nurses and Associates Annual Course
Phoenix, AZ 85001, United States

May 19-22, 2012
2012-Digestive Disease Week
San Diego, CA 92121, United States

June 18-21, 2012
Pancreatic Cancer: Progress and Challenges
Lake Tahoe, NV 89101, United States

September 8-9, 2012
New Advances in Inflammatory Bowel Disease
La Jolla, CA 92093, United States

September 8-9, 2012
Florida Gastroenterologic Society 2012 Annual Meeting
Boca Raton, FL 33498, United States

September 15-16, 2012
Current Problems of Gastroenterology and Abdominal Surgery
Kiev, Ukraine

October 4-6, 2012
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Prague, Czech Republic

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American College of Gastroenterology 77th Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV 89085, United States

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Modern Technologies in Diagnosis and Treatment of Gastroenterological Patients
Dnepropetrovsk, Ukraine

December 1-4, 2012
Advances in Inflammatory Bowel Diseases
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1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

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