Topic Review

THAI J GASTROENTEROL 2006
Vol. 7 No. 3
Sept. - Dec. 2006

Nonpolypoid Colorectal Neoplasm and Magnify Chromoendoscopy

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EXTRACT

Nonpolypoid lesion is truly existed and contains a significant proportion of advanced adenoma and cancer. Detecting this lesion is difficult and requiring meticulous work involving advanced techniques . Currently, magnify chromoendoscopy is the best tool that have the highest sensitivity for detecting nonpolypoid lesions. New techniques such as narrow band imaging (NBI), Fujinon intelligence chromoendsocopy (FICE) and virtual colonoscopy are promising but these require further investigations to support the results. The depressed lesion is the most fearful condition for every physician who deals with colon cancer detection since it contains more advanced cancer than others.

Key words : nonpolypoid, colorectal, neoplasm, chromoendoscopy, magnify

[Thai J Gastroenterol 2006; 7(3): 157-164]

INTRODUCTION

It has been accepted lately that not only polypoid lesion can grow as a colon cancer, flat and depressed lesions (nonpoypoid lesions) can also contribute a significant portion of colorectal neoplasms[1-7]. Originally, nonpolypoid lesions thought to exist only in Japan but a lot of reports on the incidence of these lesions have been published trough the world[1-7]. It is important that physician who involve in colorectal cancer detection program realized that this lesion is existed and also know how identify the lesions. The standard endoscopy is able to recognize majority of nonpolypoid lesions. However, these types of lesions are easy to be missed due to its flat in nature. To enhance the sensitivity for detection of the lesions, better techniques may be required. In addition, the slightly depressed lesions contain the highest risk of high grade dysplasia or invasive cancer when compared with typical polypoid lesion. Recently, magnify endoscope and chromoendoscopy are becoming popular techniques to facilitate the detection rate of the nonpolypoid lesions.

Classification

The original classification of colorectal carcinoma has been proposed by the Japanese Society for Cancer of the Colon and Rectum in 1997[8]. It classified the tumors into 3 types according to the morphology of

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the lesions: 1) protruded (Ip, Isp, Is); 2) superficial (IIa, IIb, IIc); 3) excavated (Figure 1). Recently, these have been simplified and reclassified to the Paris endoscopic classification. These can be grossly categorized into 3 groups; protruded or polypoid, flat, and depressed lesions (Figure 2).

It is conceivable that the nonpolypoid lesion can be separated into flat and depressed lesions. The category "lateral spreading tumor" which is described as a 10 mm or larger lesion that spreading circumferentially rather than vertically (Figure 3) has a lower potential for developing into an invasive cancer when compared with a depressed lesion (Figure 4) (2.5% vs 7.9-70%)[9]. Apart form the morphological type of colorectal neoplasm, the risk of invasive cancer is higher if the size of lesion is larger. However, the chance of invasive cancer is highest for the depressed lesion when compared with a flat lesion (Table 1)

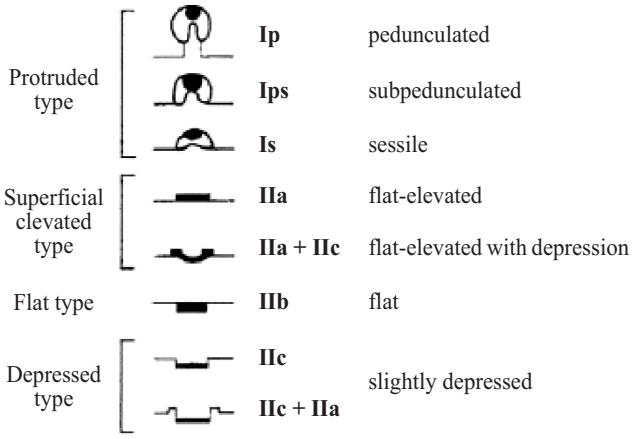

Figure 1 Japanese classification of early colorectal cancer based on macroscopic morphology

The incidences of polypoid and nonpolypoid lesions in Japan were reported to be 55.5% and 44.5% respectively[10]. The depressed lesions accounted for 1.8-2.3% of all colorectal neoplasms[11]. However, they were responsible for one third of all colorectal cancers diagnosed. Another report from UK showed similar incidences of flat lesions and depressed lesions to be 36% and 0.6% respectively[12]. It is also noted that 75% of depressed lesion in this report contained Dukes' A cancer.

"Adenoma -carcinoma sequence" theory has been approved as a major pathway for colorectal cancer development of polypoid lesion in the West[13]. However, few witnesses of adenema-carcinoma sequence have been reported. In addition, few benign adenomatous remnants were observed in patients with colonic cancer[14,15].

Therefore, another theory called "de-novo" which claims that cancer can emerge directly from normal epithelium without going through a stage of polypoid adenoma. The supportive evidence is found in many colorectal cancers which showed nonpolypoid growth contained no adnomatous remnants[14]. Moreover, many experimenatal models in animals supported the theory of de-novo carcinogenesis of colon cancer.[16,17]

Role of chromoendoscopy

With a standard endoscopy, detecting polypoid lesion is not difficult. However, the missed rate from the standard technique is quite significant[18]. In order to discover flat or depressed lesions, many hints during endoscopy were suggested. Finding the abnormal

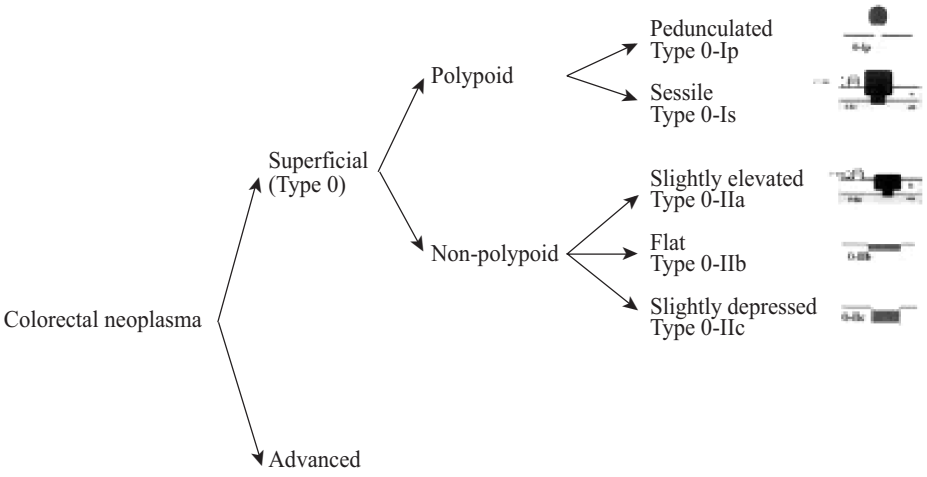

Figure 2 The Paris endoscopic classification for colorectal neoplasms.

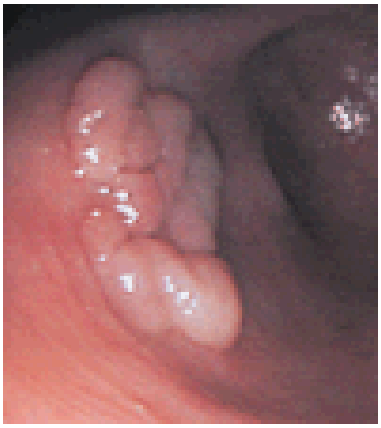

Figure 3 Demonstrating laterally spreading tumor of the colon

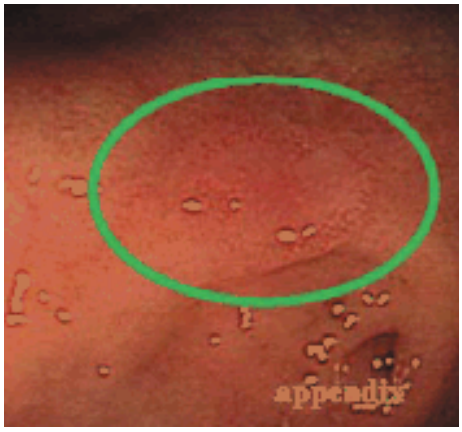

Figure 4 Demonstrating depressed lesion near the appendiceal orifice

Table 1 Risk of invasive carcinoma according to type and size of lesions

Gross appearance	Size (mm.)					Total
	≤5	6-10	11-15	16-20	≥21	
Depressed*	20/253 7.9%	70/156 44.9%	51/73 69.6%	21/24 87.5%	15/17 88.2%	177/523 33.8%
Flat-elevated	2/6,848 0.03%	3/1,197 0.25%	14/550 2.5%	22/201 10.9%	65/307 21.2%	106/9,103 1.2%
Protruded	0/6,234 0%	62/4,732 1.3%	89/1,163 7.7%	68/414 16.4%	68/233 29.2	287/12,776 2.2%
Total	22/13,335 0.16%	135/6085 2.2%	154/1786 8.6%	111/639 17.4%	148/557 26.6%	570/22,402 2.5%

(Modified from Kashida H, Kudo S. Early colorectal cancer, concept, diagnosis and management. Int J Clin Oncol 2006).

area by a careful examination is important. The important technique is looking for abnormal lesions including small area of slight color change, minimal deformation of the bowel wall, interruption of the capillary pattern and spontaneous or contact bleeding area. Unfortunately, with the limitation of white light regular endoscope, some lesions are still left undetected.

Chromoendoscopy is a technique on using the dye spray during endoscopy to detect the area of abnormal mucosa. It is very useful for clarifying the nonpolypoid lesion especially the depressed type (Figure 5). The most commonly used dye for chromo-endoscopy is diluted indigo carmine (0.1%-0.4%). This solution enhances the surface area of the lesion and surrounding mucosa. Mucosal grooves and depressed area usually pool in the dye. This phenomenon, in turn, highlights the border of the lesion and also facilitate visualization of the lesion when magnify endoscope is added to the technique. In addition, crystal violet solution can be added into the technique to enhance the picture in detail.

Methylene blue is another type of dye that can be used for this purpose. However, the effect of staining is not equivalent to indigo carmine. In addition, it is absorbed into the tissue, thus washing out the dye is a problem when its presence is no longer required.

With recent advance in endoscope manufacturing technology, the magnify endoscope is recently available. The picture of flat lesion especially after dye sprayed is unbelievably easy to find. Many studies reported the improvement of diagnostic yield form magnify chromoendoscopy compare with regular endoscopy (Figure 7)[19,20]. Hurlstone, *et al*. reported the advantage of magnify chromoendoscopy in detection of cancer for ulcerative colitis patients who underwent colonoscopic surveillance for colorectal cancer. They

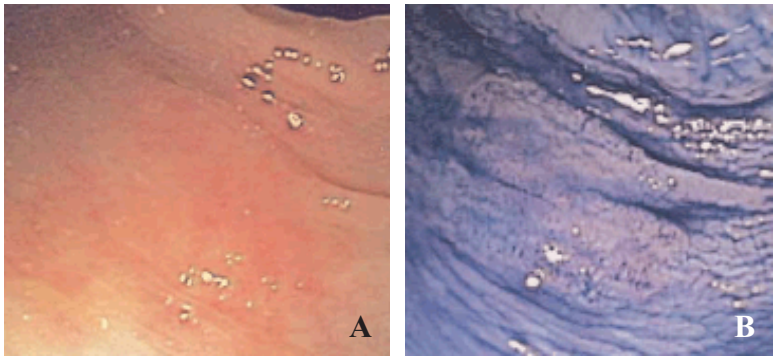

Figure 5 A A flat lesion from white light regular endoscopy
B A flat lesion can be seen much easier after indigo carmine spraying

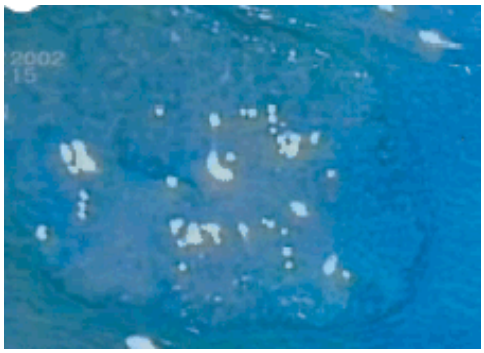

Figure 6 Methylene blue staining of the colonic adenoma

found that there were significantly more intraepithelial neoplastic lesions were detected in the magnification chromoscopy group compared with controls (69 vs. 24, P <0.0001). Moreover, more number of flat lesions with intraepithelial neoplasia were detected by this technique compared with controls (P <0.001)[19]. Additional study reported from the same group showed that the sensitivity and specificity of this technique in distinguishing non-neoplastic from neoplastic lesions were 98% and 92%, respectively[18]. Another study from Japan also supported the superior results of magnify endoscopy over the conventional technique. Konishi, *et al*., reported that the accuracy of magnifying colonoscopy in distinguishing neoplastic from non-neoplastic lesions. The accuracy from magnify endoscopy was significantly higher than non-magnifying colonoscopy (92%, 372/405 vs. 68%, 278/407)[21].

Non-staining chromoendoscopy

Newly developed systems that control the wave length of the light source by processor generated or filtering technique called Fujinon intelligence

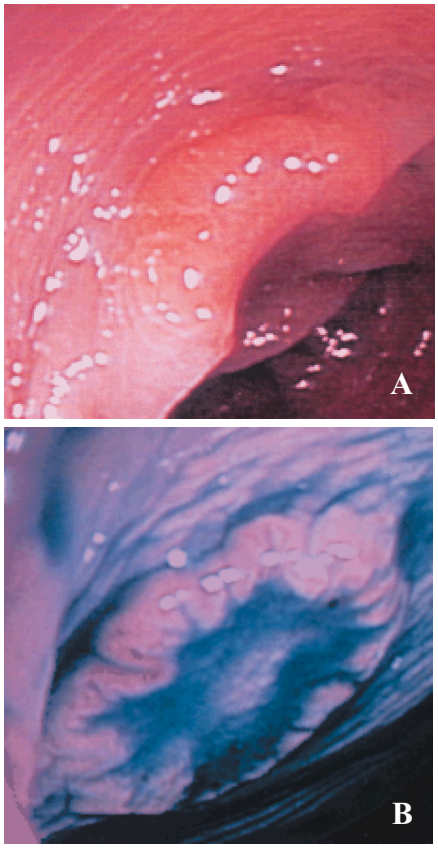

Figure 7 A A slight reddish area of depressed lesion
B Lesion can be seen clearly by the magnify chromoendoscopy

chromoendoscopy (FICE, Fujinon company) and narrow-band imaging (NBI, Olympus company) can be of help for magnification endoscopy without a need for dye spraying. The purpose of these systems is to enhance and clarify the area that containing hemoglobin especially blood vessels in the inflamed and neoplastic tissue (Figure 8).

A group form National Cancer Center Hospital

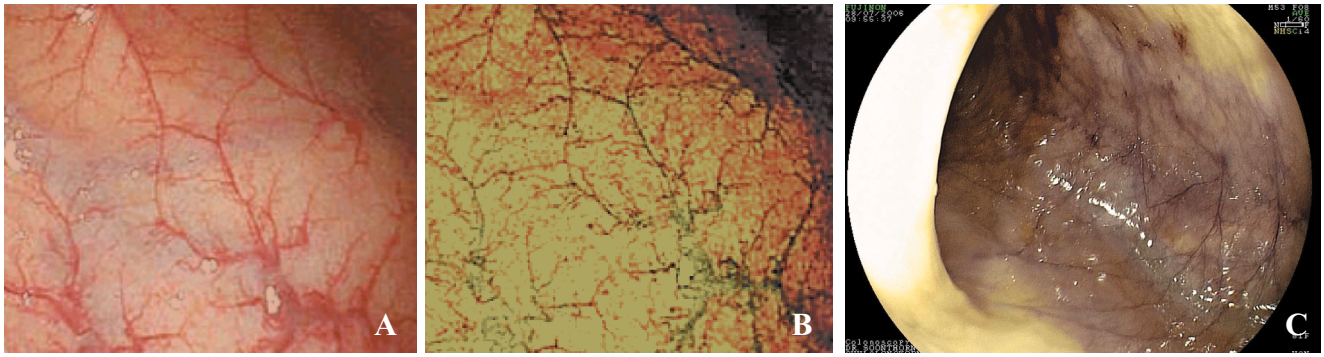

Figure 8 A Standard white light endoscopic view demonstrating thick vessels and normal vascular pattern.
B NBI image demonstrating a better visualization of fine capillaries.
C FICE image demonstrating different color but also a clear view of vascular pattern.

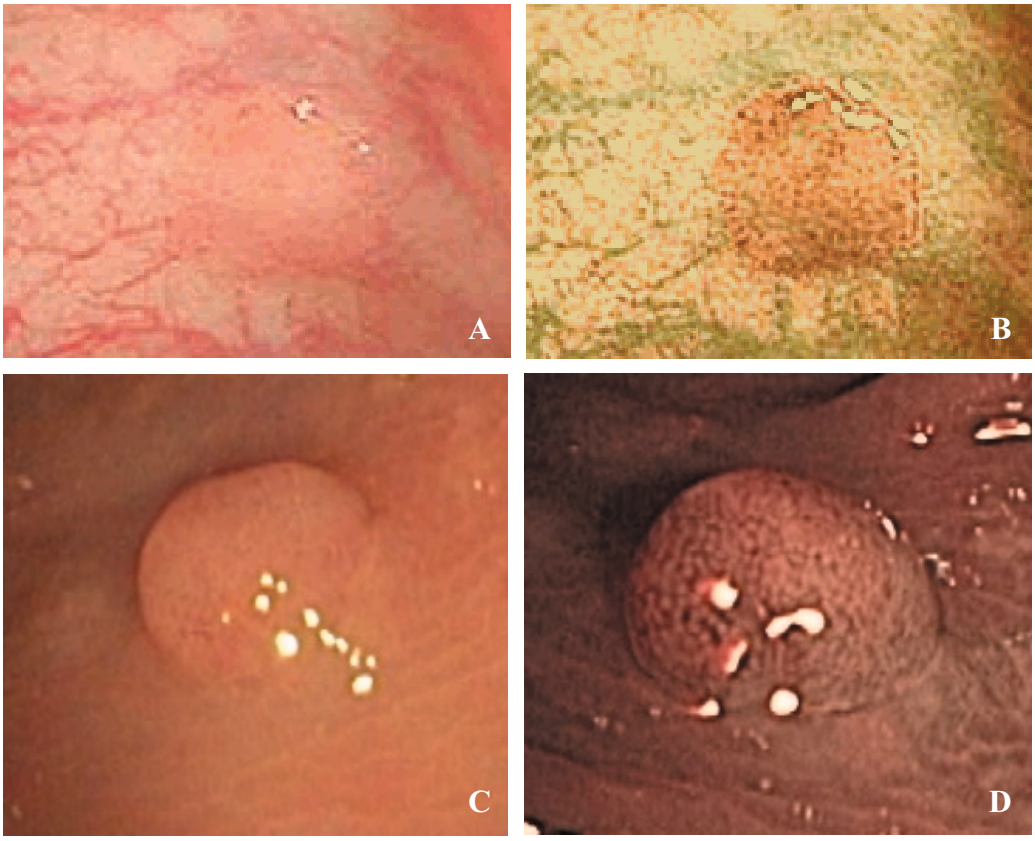

Figure 9 A A small adenoma (7mm) can be hardly seen by conventional endoscopy
B NBI image demonstrating a better border ouline of the adenoma
C Conventional ensocopy showed a small polyp
D Magnify NBI image confirms it as a hyperplastic polyp by demonstrating multiple round pit pattern.

East suggested that the NBI system provides imaging features that compatible to those of both conventional endoscopy and chromoendoscopy (Figure 9). (Table 2)

In addition, to distinguish neoplasms from non-neoplastic lesions, NBI was equivalent to chromoendoscopy (Figure 10)[22]. To date, there is no standard guideline regarding the technique for non-staining chromoendoscopy available yet. However, there is a possibility that this method may replace or be used in addition to a standard magnify chromoendoscopy to detect nonpoypoid lesions.

Table 2 Diagnostic accuracy among conventional endoscopy, NBI and chromoendoscopy

	Conventional colonoscopy		NBI colonoscopy		Chromoendoscopy	
	Nonplastic	Non-neoplastic	Nonplastic	Non-neoplastic	Nonplastic	Non-neoplastic
Histological diagnosis						
Neoplastic	29	5	31	3	31	3
Non-neoplastic	5	4	0	9	0	9
Accuracy (%)	79.1		93.4		93.4	
Sensitivity (%)	85.3		100		100	
Specificity (%)	44.4		75.0		75.0	

(Modified from: Machida H, Sano Y, Hamamoto Y, *et al*. Narrow-band imaging in the diagnosis of colorectal mucosal lesions: a pilot study. Endoscopy 2004; 36(12): 1094-8.

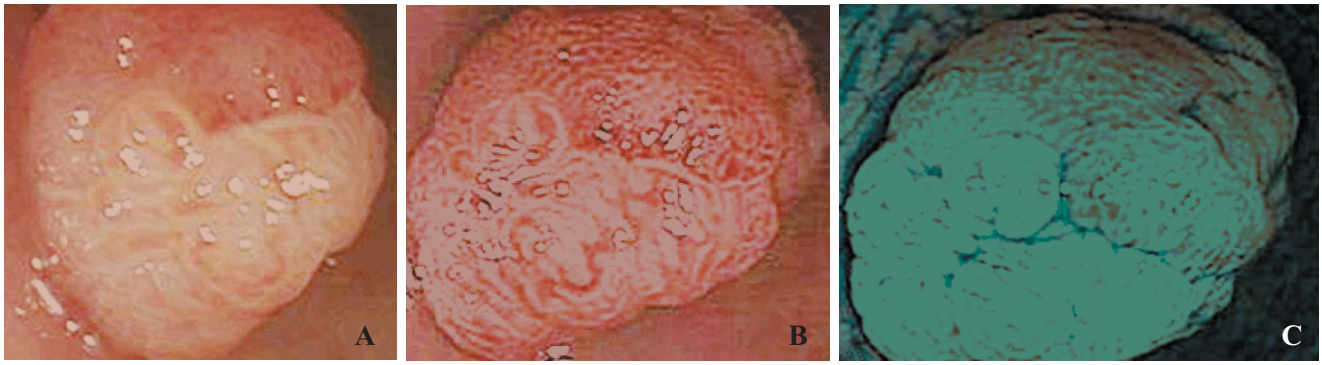

Figure 10 A White light enoscopy demonstrating a large polyp
B Better pitt pattern can be seen from NBI image
C Indigo carmine spray showing an equivalent visualization of the polyp

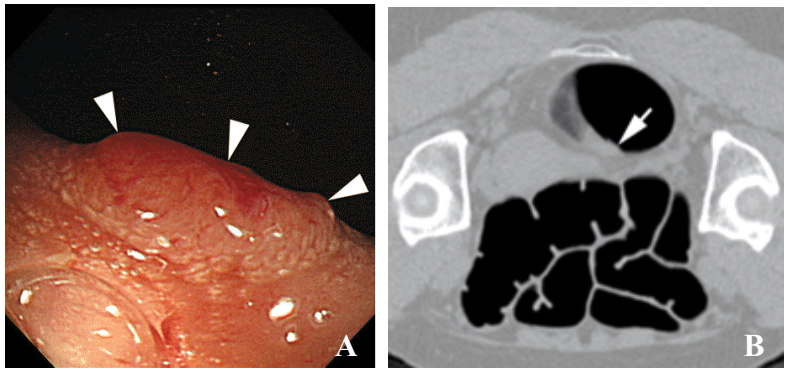

Figure 11 A A flat polyp by video-endoscopy
B 2-D transverse image of the colon demonstrates a flat polyp

Role of Virtual CT colography for nonpolypoid lesion

As described elsewhere that the CT colography has a limitation for a small polyp that less than 6 mm. in diameter[23]. There have been only a few reports regarding the role of this technique for detection of flat polyps. (Figure 11, 12)

Currently, the limitation of CT colography is sensitive for a flat lesion at least 7 mm in size and 2 mm in height[24]. Unfortunately, this technique was found to have a lower sensitivity for flat polyps than small polyps[25]. A recent study by Pickhardt *et al*, demonstrated that no histological advanced flat lesions were missed from CT colography[26]. However, the majority of those lesions were hyperplastic polyps and not a truly flat adenoma. Till now, the role of CT colography

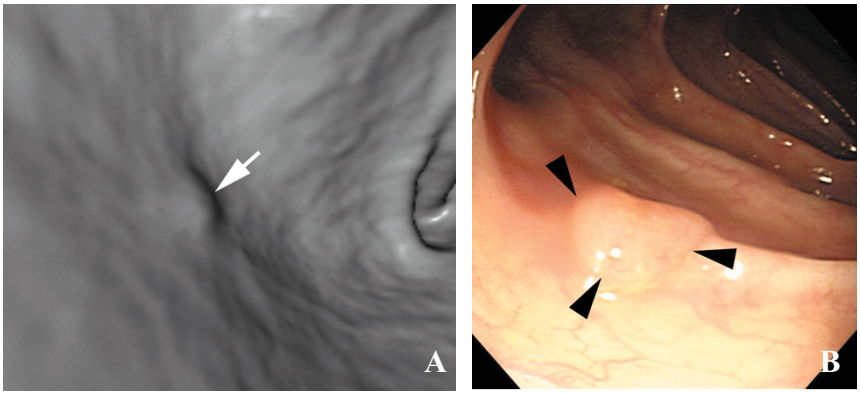

Figure 12 A 3-D endoluminal image of CT colography shows a plaquelike, slightly elevated lesion. B A corresponding lesion is seen by video-endoscopy.

for depressed lesions is unknown. The outside luminal view may have the advantage for extrinsic involvement of the depressed lesion over standard colonoscopy but this hypothesis requires more data to support.

From the latest review, it may more appropriate that first-line colorectal investigations in a screening cohort using CT virtual colonoscopy requires further clarification. More studies using a chromoscopic colonoscopy technique compare with CT virtual colonoscopy may be required to clarify the comparable diagnostic abilities of these investigatory techniques.

CONCLUSIONS

Nonpolypoid lesion is truly existed and contains a significant proportion of advanced adenoma and cancer. Detecting this lesion is difficult and requiring meticulous work involving advanced techniques. Currently, magnify chromoendoscopy is the best tool that have the highest sensitivity for detecting nonpolypoid lesions. New techniques such as narrow band imaging (NBI), Fujinon intelligence chromoendsocopy (FICE) and virtual colonoscopy are promising but these require further investigations to support the results. The depressed lesion is the most fearful condition for every physician who deals with colon cancer detection since it contains more advanced cancer than others. Again, magnify chromoendoscopy seems to be the only tool that help.

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