Narrow Band Imaging and Autofluorescence Imaging for the Detection and Optical Diagnosis of Colorectal Polyps

Kelvin Teck-Joo Thia, *MBBS, MRCP*, Chris San-Choon Kong, *MBBS, MRCP*, Choon-Jin Ooi, *MRCP, FRCP*
Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

ABSTRACT

Colorectal cancer is the most common cancer in Singapore and polyps which are detected during screening colonoscopy are routinely removed. Conventional white light colonoscopy has a substantial miss-rate for polyps and limited accuracy in differentiating neoplastic from non-neoplastic polyps. Dye-based chromoendoscopy and more recent equipment-based image enhanced endoscopic techniques such as narrow-band imaging (NBI) and autofluorescence imaging (AFI) are promising tools to improve polyp detection and optical diagnosis. Current evidence suggests that NBI may not be superior compared to high definition white-light for polyp detection, but it achieves excellent accuracy in polyp characterisation, approaching that of histopathology. AFI is a wide area scanning modality which functions as a red-flag technique to improve polyp detection, although the evidence is still evolving. The ability to accurately characterise polyps with NBI and AFI will guide the management of polyps and in some cases, avoid unnecessary polypectomy and routine histopathology. This has potential to reduce associated costs and risks of polypectomy, and improves on overall efficiency of screening colonoscopy. The review will discuss the technology, current evidence and the issues relevant to the role of NBI and AFI for the detection and optical diagnosis of polyps in colorectal cancer screening.

Keywords: autofluorescence, chromoendoscopy, colorectal polyp, optical diagnosis, narrow band imaging

INTRODUCTION

Colorectal cancer (CRC) is the most common cancer in Singapore for the past 8 years. The age-standardised rates for men for the period 2003–2007 was 40.5 per 100,000 per year and for women, it was 29.0 per 100,000 per year[1]. Epidemiological data from the Singapore Cancer Registry also revealed that CRC incidence had increased by two-fold in the period 1993–1997 compared to 1968 to 1972[2]. The life-time risk of CRC for the average Singaporean is about 1 in 55 and each year about 1,500 new CRC cases are diagnosed in Singapore. The recommended choices of CRC screening based on guidelines from the USA, the UK, Canada, the Asia Pacific and the recently published National Clinical Practice Guidelines for the average risk individual include faecal occult blood test (FOBT), flexible sigmoidoscopy and colonoscopy[3,4]. There is as yet no national population screening programme for CRC in Singapore but opportunistic screening occur in public polyclinics, family practitioners, the Singapore Cancer Society and at specialist clinics in hospitals[5].

Prevention of CRC with early detection and removal of adenomas (pre-cancerous polyps) have been the central goal of screening programmes, and colonoscopy is considered the gold standard method. The effectiveness of colonoscopy in reducing CRC incidence depends on adequate visualisation of the entire colon which depends on good quality bowel preparation as well as diligence in inspection of mucosa with adequate withdrawal time[6,7]. Despite the best of efforts to carefully examine the colon, studies have demonstrated that even experienced gastroenterologists may miss up to 6% of advanced adenomas and 30% of all adenomas[8,9]. The presence of small, flat and depressed neoplastic lesions can be particularly challenging to detect using standard white light endoscopy[6].

An approach to improve on polyp detection rate is through contrast enhancement of colonic mucosa. For the past 3 decades, dye-based chromoendoscopy has been in use although mainly confined to specialised centres. More recently equipment-based electronic chromoendoscopic methods such as narrow-band imaging (NBI) and autofluorescence imaging (AFI) appear to be promising techniques of endoscopic examination. In this review, we will discuss the technology, current evidence for dye-based chromoendoscopy, NBI and AFI, as well as their potential use in the detection and differentiation of colorectal polyps within the context of colorectal cancer screening.

DYE-BASED CHROMOENDOSCOPY

Technology

Dye-based chromoendoscopy had been in use since the 1970s often with magnification function to enhance colonic surface structures. These staining agents are generally inexpensive, safe to use and are delivered via a spray catheter. Pre-treatment of the mucosa with mucolytic agent to disrupt and remove excess mucus helps improve visualisation but is not essential before application of dyes. In the colon, dye-spraying with indigo carmine or methylene blue allows pooling of dye in the crypt openings or edges to better delineate crypt patterns, otherwise known as pit patterns.

Current Evidence

Polyp Detection

One of the major aims of dye-based chromoendoscopy had been to identify small and flat polyps which may be missed in conventional colonoscopy. In a Cochrane meta-analysis[10] of 4 prospective studies[11–14], there was a superior adenoma detection rate observed with chromoendoscopy compared with conventional white light colonoscopy, with the former yielding significantly more patients with at least 1 neoplastic lesion with an odds ratio of 1.61 (95% CI 1.24–2.09).

Polyp Differentiation

One of the most established colonic pattern classification systems known as the Kudo classification has achieved a high level of accuracy (> 90%) for the characterisation of polyp type in expert hands. The inter-observer and intra-observer variability for Kudo classification of polyps is also acceptable. In some tertiary Japanese centres, diminutive polyps (polyp size <5mm) are left in situ without further histopathologic evaluation if there were no neoplastic features, and if the patient agreed to return for colonoscopic follow-up[15].

Limitations

While dye-spray chromoendoscopy is widely practised in Japan and there exists good evidence for its improved detection abilities and optical assessment of polyp histology, there has been reluctance among gastroenterologists elsewhere to adopt this technique for CRC screening. The reasons are mainly due to the time-consuming nature of this technique which can prolong procedural time by two- to three-folds[12,13]. Further hindering its widespread adoption into clinical practice is the steep learning curve associated with interpretation of chromoendoscopic images for polyp diagnosis. One study suggested that 200–300 histologically confirmed lesions were needed to achieve proficiency in polyp characterisation[16]. Furthermore if magnification function is combined with dye-spray chromoendoscopy (a practice more prevalent in Japan than in the West), manual adjustment of lens to achieve a sharp image could make the procedure more tedious because of movement associated with peristalsis and respiration.

NARROW BAND IMAGING (NBI)

Technology

NBI is a novel blue light endoscopic technique which alters the wavelength of illumination light used, making the centre wavelength shorter compared to standard white light. Under NBI, the superficial structures in mucosa such as microcapillaries are selectively highlighted due to the shallower penetration of mucosa with blue light[17,18]. Endoscopic examination with NBI is carried out in the usual way, without any special preparation needed. The NBI mode can be conveniently activated through a button on the scope handle and most commercially available endoscopic units have magnification function up to 100x, as compared with 30x for standard endoscopy using a 20-inch monitor[19]. Neoplastic tissue is characterised by increased angiogenesis, and so adenomas typically appear darker due to increased microvessel density compared with normal mucosa[20].

Current Evidence

Polyp Detection

There have been many studies comparing NBI with white light examination[21–26], with earlier studies demonstrating some improvement in detection rate as well as a possible learning effect induced by NBI which enables endoscopists to better detect polyps using conventional white-light colonoscopy[23,27]. However in the largest randomised trial to date involving 1,256 patients undergoing screening colonoscopy by 6 examiners in private practice, there was no difference in the adenoma detection rate between NBI and high definition white light[22]. It is unclear if NBI would perform better compared to standard white light endoscopy which is the current prevalent endoscopic system in clinical practice. Furthermore, optical settings of NBI enhancement function may influence detection abilities and may account for differences in outcomes from various studies[28].

Polyp Differentiation

Conventional white light colonoscopy has limited accuracy in differentiating neoplastic from non-neoplastic polyps in the range of 60–80%[18,29,31]. Many studies have explored the use of NBI (with and without magnification) in optical diagnosis of polyp, compared to white light and dye-based chromoendoscopy, and have generally reported favourable performance characteristics of NBI[31–35]. Studies evaluating the use of NBI for the optical diagnosis of polyps are based on either pit patterns and/or microvascular appearance on the polyp for classification into neoplastic (adenoma) or non-neoplastic (hyperplastic) polyps. In a recent trial designed to assess whether optical diagnosis was safe and feasible in routine clinical practice, researchers from St Mark's hospital in the UK reported an overall accuracy for polyp characterisation at 0.93 (95% CI 0.89–0.96) for polyps <10mm in size[36]. Relying on optical diagnosis alone, the surveillance interval after colonoscopy would have been correctly recommended for 98% of patients according to British guidelines, thus making a strong case for dispensing with routine histopathology.

AUTOFLUORESCENCE IMAGING (AFI)

Technology

AFI is an innovative endoscopic technique based on the principles of tissue excitation with a shorter wavelength which leads to emission of a longer wavelength of light. It does not require injection of fluorescence drugs and AFI is able to detect subtle differences in the concentration of endogenous fluorophores in tissues[37]. Malignant transformation of tissue has been associated with the emission of relatively longer wavelengths of light (with a shift from green appearance to purple)[38]. The composition of emitted autofluorescent light has been shown to vary between adenomas and non-neoplastic polyps and can be used for differentiation during endoscopy, with adenomas appearing as purple compared to normal green mucosa[39,40]. As the AFI modality provides inspection of large areas of mucosa at a given time, it can also serve as a red-flag scanning technique for polyp detection[37].

Current Evidence

Polyp Detection and Differentiation

Unlike NBI, research in the use of AFI for colorectal polyp detection and diagnosis are relatively fewer. In a pilot study with 75 polyps assessed, AFI demonstrated a superior ability at polyp characterisation compared with white light[41], with a sensitivity of 85% and a specificity of 81%. However, the main limitation with this prototype AFI fiber-optic system was the low-quality images produced and the highly variable level of background fluorescence among patients. In another small study, a video-enabled AFI system showed early promising results with improved quality of images obtained at endoscopy, and better detection capability compared to conventional white light[42,43]. More recently, AFI and NBI modalities were incorporated into a single video-endoscopic system with high definition white light, and this new trimodal endoscopic system is currently undergoing evaluation in many clinical centers.

In the only randomised controlled trial comparing AFI with white light, AFI did not reduce the adenoma miss rate significantly. However the patient population screened in this study was heterogenous (included non-polyposis colorectal cancer syndrome) and as such may not be generalised to the normal at-risk population. The ability of AFI to distinguish adenomas from non-neoplastic colonic polyps real-time was unsatisfactory with a diagnostic accuracy of 63%[44]. There is a possibility that combining both AFI and NBI information on polyps in a diagnostic algorithm, may help to improve on the optical diagnostic accuracy of polyp histology[45].

As the AFI image quality available with current video endoscopy is still inferior to high definition white light endoscopy, it is unlikely to be applied as a stand-alone technique for polyp detection[37]. Further studies are needed to determine the accuracy of AFI alone and in combination with NBI, particularly in the real-time endoscopic diagnosis of polyp.

NBI AND AFI FOR OPTICAL DIAGNOSIS OF POLYPS: PROS AND CONS

With recent advances in endoscopic imaging which offer high resolution, high-definition quality images, smaller polyps (<10mm) are more frequently encountered. The conventional approach in colorectal polyp management would be to resect all raised mucosal lesions irrespective of size or appearance. However, the majority of polyps encountered in screening colonoscopies are <10mm and at least half these polyps are non-neoplastic such as hyperplastic polyps[6,46]. There is now emerging evidence to challenge the current dogma in the endoscopic management of colorectal polyps[47,48].

By using NBI and AFI to accurately diagnose polyp histopathology, we can potentially avoid unnecessary procedures to remove non-neoplastic polyps, and thus reduce the associated risks of polypectomy. Similarly, routine small adenomatous polyps could be removed and disposed of without need for formal histopathology as such polyps are unlikely to harbour malignant cells[32]. Other potential areas of clinical use would be in patients receiving anti-platelet and anti-coagulation, for which polypectomy is deemed unsafe to perform, and in such a scenario, both NBI and AFI could guide the endoscopist in the subsequent management of the polyp. Perhaps a point understated, the ability to perform optical diagnosis is also useful, as a portion of polyps (8–19%) may be lost or uninterpretable secondary to diathermy effect during polypectomy[49].

The optical diagnosis of polyp with NBI and AFI to replace formal histopathology is still not ready for routine practice until several important issues have been addressed. There is a need to establish NBI and AFI defined endoscopic criteria for real-time endoscopic diagnosis of polyp. It is likely that an integration of "confidence level" into the clinical interpretation of polyp would be needed since not all polyps will demonstrate all distinctive NBI and AFI mucosal features[50,51]. Thus when "high confidence" hyperplastic polyps are encountered, they can be left in situ, and when small "high confidence" adenomas are diagnosed optically, they can be resected and discarded without histopathology. Polyps which cannot be classified with "high confidence" can still be resected but should undergo histopathologic analysis. This approach while cautious will enable both reduction in unnecessary polypectomy and costs associated with histopathology as well as prevent significant problems of misclassification[49].

Many of these image enhanced endoscopic studies on optical diagnosis of polyps were performed in tertiary centres, and there is a need to ascertain if endoscopists in the community and in non-specialised settings are willing to undergo training to obtain the necessary accreditation. Quality control programmes for endoscopists will have to be developed whereby a fraction of polyps are regularly submitted for microscopic confirmation to ensure acceptable standards of diagnostic accuracy[49]. Perhaps one of the major difficulties with NFI and AFI prediction of polyp histopathology would be in the assessment of sessile serrated adenomas. These polyps have mainly architectural features of hyperplastic polyps but also have some cytologic and biologic features of classic adenomas[52]. The performance characteristics of NBI and AFI have yet to be established for sessile serrated adenomas (SSA), and one study suggested that the presence of SSA could negatively influence the accuracy of NBI[45]. Until stronger evidence is established for the optical diagnosis of polyp to replace formal histopathology, extreme caution should be exercised when considering "non-removal" of polyps, in view of potential medico-legal issues arising from error in diagnosis and inadequate polyp treatment.

The recent introduction of probe-based confocal endomicroscopy applied in conjunction with NBI and AFI techniques can enable a much more precise visualisation of GI mucosa, with up to 1,000-fold magnification view of surface epithelium and vascular patterns during video endoscopy[53,54]. This new technology allows for high resolution real-time histological imaging of colonic mucosa, resulting in a virtual or optical sectioning of the tissues examined with high degree of accuracy akin to histopathology[55,56]. The application of probe-based confocal endomicroscopy in complementary fashion to NBI and AFI, has the potential to definitely diagnose "indeterminate" polyps such as sessile serrated adenomas.

CONCLUSION

It is envisaged that the role of screening colonoscopy in Singapore will expand as the public becomes more aware of the importance of colorectal cancer screening. As local gastroenterologists and surgeons strive to meet the increasing demands of screening colonoscopy, there should also be ongoing efforts to improve on the quality and efficacy of this screening modality. There is good evidence to support the role of NBI for the characterisation of colorectal polyps but NBI does not appear to enhance polyp detection over high definition white light. There is great potential for image enhanced optical diagnosis of polyps to improve on the efficiency of screening colonoscopy. However further validation studies across centres and among endoscopists of varying experience are still needed, to confirm the performance characteristics of NBI and AFI for the differentiation of polyps.

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