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Thailand Colorectal Neoplasm and Surveillance

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ABSTRACT

Over the last decade, screening for coloneoplasm has become a standard of case for western countries. In Thailand due to a lower incidence of colonic cancer and financial constrain, screening for Thai is strie an optional test. Currently, screening is only recommended for one with increased risk.

This article is focus mainly on new investigations and quideline for increased risk patients.

Key words : Colorectal neoplasm, screening, surveillance

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INTRODUCTION

Over the past decade, screening and surveillance of common malignant cancers have become a routine health promotion in Thailand. Colorectal neoplasm is among one of them but standard of practice for this screening and surveillance is still controversial. Target population is still undecided. In addition, tests to be used are varies.

Recent evidences from Asia demonstrated that incidence of colorectal cancer in this part of the word is rising compared to 30 years ago[1,2]. Generally, early case of colorectal neoplasm is asymptomatic, there fore investigating only symptomatic individual may be too late. The standard tool for work up is mainly colonoscopy. Unfortunately, colonoscopy is not widely available for all in Thailand. Lack of man power is the main culprit. Moreover, insufficient financial support from the government can lead to inadequate supply of the service.

Stool occult blood in one of the popular tool for screening this type of malignancies but apply this test for Thais may have a very low yield since positive predictive value from stool occult blood is expected to be low. This may be due to the low incidence of colorectal cancer. Further more, there is a high false positive rate from a high prevalence of peptic ulcer diseases in Thailand.

This article is focus mainly on screening and surveillance for population at higher risk than average.

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METHODS AND TOOLS FOR SURVEILLANCE AND SCREENING

1. Stool occult blood

As mentioned earlier for a possibility of a low positive predictive yield from stool occult blood test, we can not recommend a routine surveillance for colorectal neoplasm in Thai citizen at this moment. However, many physicians still elect to perform it since it is an easy and inexpensive test. With rehydration technique the sensitivity will be better but unfortunately the specificity will drop. It has been recommended that patient should have at least 3 specimens performed. They also need to avoid consumption meal or medications that can alter peroxidase activity such as red meat, and vitamin C[3].

Patients with a definite diagnosis such as iron deficiency anemia should undergo for a more specific investigation such as endoscopy. One with high risk family history should not wait for the result of stool occult blood test.

2. Sigmoidoscopy

The examination will cover the area from anus up to 60 centimeters of sigmoid colon. It has been noted from previous studies that sigmoidoscopy can reduce the mortality rate from colorectal cancer[4-7]. However our recent study has found that majority of cancers were beyond the reach of sigmoidoscope[8]. Moreover, this type of scope is not widely available in Thailand. Rigid sigmoid oscope is also not popular due to its inconvenience. However if the test is performed, the patient will need to go for a complete colonoscopy if large polyps or villous adenoma are discovered[9-11].

3. Colonoscopy

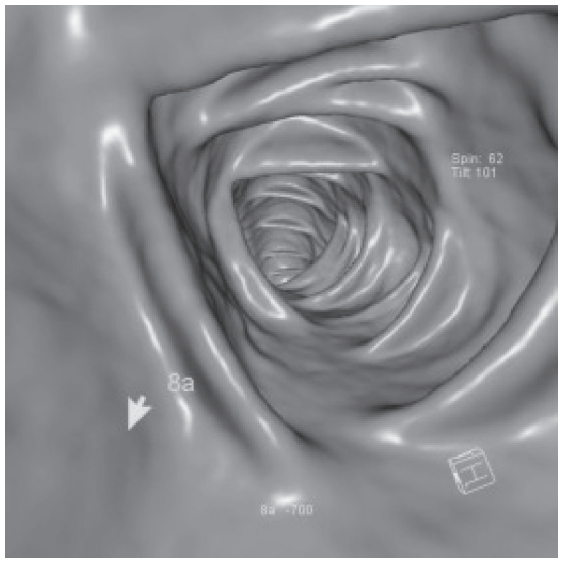
Currently, colonoscopy is a standard test for colorectal cancer screening worldwide. The major benefit from this test is its capability to remove polyp whenever detected. The disadvantage points are mainly related to sedation and bowel preparation. The missed rate form colonoscopy was reported to be around 6%[12]. Usually if the first colonoscopy is normal, there is no need for another colonoscopy until next 10 years. Rex *et al* reported less than 1 % polyp detection rate at 5 years after a normal complete colonoscopy[13].

4. Double Contrast Barium Enema (DCBE)

This is an alternative test for colonoscopy. It can detect a large polyp or cancer by having sensitivity at 85% compared to colonoscopy (95%)[14] American Gastroenterological Association (AGA) recommended it as a standard test without need for sigmoidoscopy[15]. In author's opinion, it may be inappropriate for Thais. Our rectal cancer rate is still slightly higher than Caucasians. Therefore sigmoidoscopy is needed as a supplement test if patients elect to have DCBE as a primary test.

5. Virtual Colonoscopy

This is a new kid on the block who just came out and has potential to substitute for DCBE. The technique involves with spiral CT scan with special software. Patient still requires bowel preparation but no



Fugure 1 Normal colon by 3D virtual colonoscopy

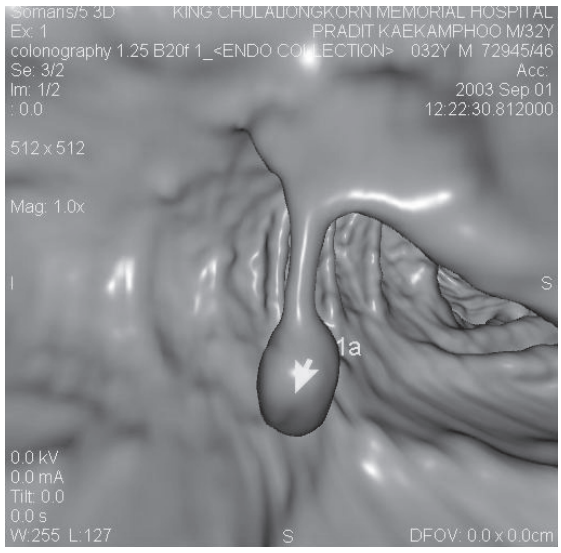


Figure 2 A peduculated polyp from virtual colonoscopy

need for sedation or intravenous contrast injection. Time to read and reconstruct pictures is around 90 minutes. Pictures will be displayed as 2-D and 3-D with or without fly-trough motion (Figures 1 and 2). Another advantage is backward fly-trough to detect behind the fold lesion. The sensitivity and specificity of virtual colonoscopy compared to colonoscopy are 90% and 85% respectively[15].

6. Stool for DNA

It is becoming a promising test by testing genetic material from stool. However majority of the tests are under research protocol. The overall sensitivity reported to be around 70-90% for colorectal neoplasm[16].

Colorectal Cancer Screening in Patients at Increased risk

The risks for colorectal cancer are different among persons who have family members with colorectal neoplasm. The more, the younger and the closer of family members to that person convey to the higher risk of that person to have colorectal cancer. For example, one with a first degree relative with colorectal cancer before 50 years contains risk as high as 4 times of normal population. In contrast, the risk will be lower if only one second degree relative with colorectal cancer at the age after 50 was found.

Currently there is no formal study reported from our country regarding how to screen patient with increased risk. This recommendation is mainly adapted form AGA guideline in 2003[15].

There are 4 scenarios for patients with increased risk for colorectal neoplasm.

1. One with a first degree relative with colorectal cancer detected after age of 60 years. A standard colonoscopy started at 40 years every 10 years if normal is recommended.

2. One with two second degree relatives with colorectal cancer. A standard colonoscopy started at 40 years every 10 years if normal is recommended.

3. One with at least 2 first degree relatives with colorectal cancers. A standard colonoscopy started at 40 years every 5 years if normal is recommended.

4. One with first degree relatives with colorectal cancer detected before age of 60 years. A standard colonoscopy started at 40 years or the relative age minus 10 years whichever comes first and followed up colonoscopy every 5 years if the first one is normal is recommended.

5. One with only one second or third degree relative with colorectal cancer at any age. A standard colonoscopy can be performed after 50 years of age (the same as normal population).

Family Screening for Hereditary Colorectal Cancer

Hereditary colorectal cancer accounts for only less than 10 % of overall colonic cancer patients. These patients can be easily categorized into 2 groups

1. Familial adenomatous polyp (FAP) and related syndromes such as Gardner and Turcot

2. Hereditary nonpolyposis colorectal cancer (HNPCC)

Familial adenomatous Polyp (FAP) These patients usually contain multiple polyps starting from the rectum. Polyp number is usually more than 100, sometimes covering as carpet liked mucosa. Sibling of affected person can inherit this gene by 50% since it conveys by autosomal dominant pattern. Generally, polyp can be detected after 16 years of age and cancer will appear before patients turn to forty.

Screening should begin at the age of 10-12 years with sigmoidoscopy with repeat examination every year. Whenever carpet of polyps is discovered patients need to undergo total colectomy. In addition, side-view duodenoscopy is needed to screen for ampullary adenoma.

Some patients may have polyps more than 20 but less than 10. This group can be classified as attenuated adenomatous polyp coli (AAPC). The cancer usually develops 10 year later than typical FAP. Therefore, these patients can undergo for screening later at the age of 20 years. Since there is a possibility of polyp distributing in the area beyond the reach of sigmoidoscope then colonoscopy is the preferred test.

Currently, genetic test has become available. FAP related DNA can be detected from white blood cell of patients. The recommendation is to use this test in family members of patient who is less than 40 years. But the affected patient has to be confirmed as a FAP gene carrier then the rest of family members can go for the blood works. Family members with positive test result should undergo for a screening sigmoidoscopy with the same protocol as mentioned earlier. A person with negative test result needs no further work up.

Hereditary nonpolyposis colorectal cancer (HNPCC) This syndrome is also transmitted by autosomal dominant pattern. In addition to more right

sided colonic cancer, patient and family members who inherited these genes have a high chance to develop other cancers such as endometrium, small bowel, ureter, ovary, stomach and hepatobiliary systems.

Since the tumors are mainly located in the right sided of colon then screening only by sigmoidoscopy is inadequate. Patient who is at risk should undergo colonoscopic surveillance every 2 years after the age of 20 years. Identifying patient who is at risk is much more difficult than FAP related family due to more than one abnormal mismatch repair (MMR) genes have been discovered. Moreover, the rigid Amsterdam criteria can identify only 30 % of persons who are at risk (Table 1). Therefore a more flexible Amsterdam II and Bethesda guideline are helpful to increase the chance in detecting gene carriers (Table 2 and 3).

Once the person with colonic cancer or HNPCC related cancers has been identified then their blood or tumor tissue can be analyzed for MMR genes. The tumor tissue has to undergo to the process called "microsatellite instability test". The test will label whether that tumor is containing MMR gene or not.

Once the MMR gene has been identified, the rest of family members can undergo for that abnormal MMR gene test. One who is carrying that gene has to go for colonoscopy surveillance program. The rest who is negative for MMR gene can be excluded from surveillance program.

The surveillance of patients with history of polyp or cancer of the colon

1. Colonic polyp patient Up till now, there is not enough data from our country to be referred as a guideline for polyp surveillance. According to AGA guideline in 2003, colonoscopy can be performed 5 years after complete polypectomy. Patients who have incomplete colonoscopy or large polyp with or without invasive cancer at the tip should undergo repeat colonoscopy earlier within 1 year. Colonoscopy has to be performed at 3 years in patient with multiple adenomatous polyps, pedunculated polyp larger than 1 centimeter and villous adenoma containing polyp.

2. Colonic cancer patient After complete resection of colonic cancer, the chance of having anastomosis recurrent is very low.

Shoemaker *et al* reported that follow up colonoscopy has a chance to detect recurrent tumor by 2 %. Unfortunately all detectable recurrent tumors were unresectable[17,18]. This may represent under staging and incomplete resection of the tumor at the initial operation.

Table 1 Amsterdam criteria

Amsterdam Criteria[67] (for Clinical Identification of HNPCC)
At least 3 relatives with colorectal cancer plus all of the following:
One affected patient is a first-degree relative of the other two
Two or mor succesive generations affected
One or more affected relative received colorectal cancer diagnosis at age <50 years
FAP excluded
Tumors verified by pathologic examination

Table 2 Amsterdam II criteria

Amsterdam II[67] (Criteria for Clinical Identification of HNPCC, modified to take into account the increased occurence of cancer other than the colon and rectum)
At least 3 relatives with an HNPCC-associated caner (colorectal cancer and cancer of the endometrium, small bowel, ureter, or repelvis)[a] plus all of the following:
One affected patient is a first-degree relative of the other two
Two or mor succesive generations affected
One or more affected relative received colorectal cancer diagnosis at age <50 years
FAP excluded in any case of colorectal cancer[a]
Tumors verified by pathologic examination

Table 3 Bethesda guideline

Bethesda Guidelines[68] (For identification of patients with colorectal tumors who should undergo testing for microsatellite instability)

- B1 - Individuals with cancer in families that meet the Amsterdam Criteria
- B2 - Individuals with 2 HNPCC-related tumors including synchronous and metachronous colorectal cancer or associated extracolonic cancer (endometrium, ovarian, gastric, hepatobiliary, or small-bowel cancer or transitional-cell carcinoma of the renal pelvis or ureter
- B3 - Individuals with colorectal cancer and a first-degree relative with colorectal cancer or HNPCC-related extracolonic cancer or a colorectal adenoma; one of the cancers diagnosed at age <45 years,[c] and the adenoma diagnosed <40 years
- B4 - Individuals with colorectal cancer or endometrial cancer diagnosed at age <45 years[b]
- B5 - Individuals with right-sided colorectal cancer with an undifferentiated pattern (solid, cribriform) on histopathology diagnosed at gae <45 years[b] (solid or cribriform), defined as poorly differentiated for undifferentiated carcinoma composed of irregular, solid sheets c large eosinophilic cells and containing small gland-like spaces
- B6 - Individuals with signet-ring-cell type colorectal cancer diagnosed at age <45 years[b] (composed of >50% signet-ring cells)
- B7 - Individuals with adenomas diagnosed at age <40 years

In patient who colonoscopy can not be complete, a follow up colonoscopy has to be performed within six months after primary anastomosis. If there is no detectable tumor left then repeat colonoscopy can be performed at 3 and 5 year intervals.

Colonoscopic Surveillance in inflammatory bowel patients The recommendation for Crohn's disease and ulcerative colitis related cancer screening are the same. The chance of developing cancer is depend upon extension of colitis and duration of the diseases. The severity of the diseases is usually not important. Patient with pancolitis needs a surveillance colonoscopy after 8 years of diagnosis. Patient with only left sided colitis can have surveillance colonoscopy after 15 years. Some experts believe that majority of patients with left sided colitis might have microscopic colitis in the other side. Therefore, they prefer to screen their patients at 8 years instead of 15 year after establishing diagnosis.

The standard protocol for surveillance colonoscopy is random biopsy at 4 quadrants in every 10 centimeters of colon. Generally, at least 60 minutes is required for the procedure. Patient who is found to have high grade dysplasia or cancer has to undergo for total colectomy. Recently, a group from ST Mark hospital in London which is a referring center for colorectal diseases in UK has shown that performing biopsy from only suspicious lesions may be enough to detect early cancer. The have found that 110 neoplastic areas were detected in 56 patients: 85 (77.3%) were macroscopically visible at colonoscopy, and only 25 (22.7%) were macroscopically invisible. The frequency of cancer in patients who had endoscopic resection of neoplasia did not differ from that for the surveillance population as a whole (1/40 vs. 18/525; p = 1.0)[19].

In conclusion, screening and surveillance for colorectal neoplasm for Thais are still waiting for more studies from our own. Current practice is usually developed or adapted from US or European guidelines. Recommending screening for everybody at this moment is impossible due to financial constrained. Selecting one who has significant risk requiring vigilance history taking especially family risk factors. New tool for diagnosis such as virtual colonoscopy and stool for DNA test have risen as new tools but this is still not yet the substitute test for colonoscopy.

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