Colorectal Polyp: Evaluation, Management and Its Role in Gastrointestinal Tract Malignancy

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ABSTRACT

Colorectal polyp is one of important factors that have roles in developing malignancy of lower gastrointestinal tract. Adenomatous polyp is the most common colorectal polyps and it has been known as a lesion precursor for transformation process in developing gastrointestinal malignancy. Such transformation is known as adenocarcinoma sequence, a long-term process which usually does not elaborate any symptoms and remains asymptomatic. Since most colorectal polyps are asymptomatic, they are usually undiscovered at the time of diagnosis and results to the increasing case of malignancy especially the colorectal cancer.

Considering that colorectal cancer still becomes one of the most common causes of death and morbidity worldwide, early detection and elimination of colorectal polyp may have a significant role in preventing lower gastrointestinal tract malignancy.

***Keywords**: polyp, colorectal polyp, adenomatous polyp*

INTRODUCTION

Colorectal polyp is an abnormal growth of tissue or a tumor, projecting from a mucous membrane found in the colon. Colorectal polyps are uncommonly associated with symptoms. However, it may occasionally cause symptoms such as rectal bleeding, abdominal pain, and when the size is extremely large then obstruction symptom may occur. Their shapes, sizes, and type of surfaces may various. If it is attached to the surface by a narrow elongated stalk, we call it as pedunculated polyp. If no stalk is present, we call it sessile polyp. Although some polyps may be identified macroscopically, however, histopathological examination should be performed to confirm the precise type of polyp.[1,2,3]

Polyps have been known as one of important factors that potential in developing lower gastrointestinal tract malignancy, particularly the adenomatous polyps (neoplastic polyps). Therefore, histopathological examination becomes significant in clinical setting to recognize such malignancy potential. Screening assessment may also be helpful in early detection of premalignancy lesion.[2,3,4] Prompt management of colorectal polyps needs a comprehensive knowledge of clinical manifestation, anatomy, and physical examination related to their various histopathological types. Although most of colorectal polyp cases develop sporadically, but in some cases they may be found related to hereditary disorder, such as Familial Adenomatous Polyposis (FAP), Peutz-Jegher, Juvenile polyposis syndrome or Hereditary Nonpolyposis Colorectal Cancer (HNPCC).[1,2,4]

Colorectal cancer still becomes one of the most common malignant cause of death and morbidity (± 135,000 new cases were found in United States in 2001 and it was related to 57,000 deaths). Early detection and elimination of polyps may have a very significant role in preventing lower GI tract malignancy incidence.[1,4]

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PREVALENCE

The prevalence of colorectal polyps may be very various between each area. Autopsy studies and colonoscopy survey in the United States demonstrate that the prevalence ranges between 40-50%. Two third of colorectal polyp cases are adenomatous. Such prevalence is in line with the number of colorectal cancer incidences in the area, which also shows its strong correlation to the gastrointestinal tract malignancy.[2,4,5]

Histopathologicaly, colorectal polyps can be classified into categories such as neoplastic polyp, non-neoplastic polyp and submucosa polyp. Despite its potential capacity of becoming malignant, most of adenomatous polyps are usually benign at the time of detection. They are different from the non-neoplastic polyps (hyperplastic, mucosa, inflammatory polyp and hamartomatous polyp) which usually do not have any potential capacity to become malignant. Finally, the last category is submucosa polyps (such as lymphoid, lyphoma, etc). By its origin, polyps are classified as epithelial and non-epithelial polyps.[1,2,3,6]

Neoplastic Polyps (Adenomatous Polyps)

Adenomatous polyps and hyperplastic polyps are the most commonly found colorectal polyp with a prevalence of 80-90%. The important clinical significance of adenomatous polyps is its potential capacity of becoming malignant which will develop into cancer by a process called adenoma-carcinoma sequence.[1,2,3,7]

Colorectal adenoma mostly found in community population. A study conducted by autopsy method showed that its worldwide prevalence is about 22-60%. Whereas a colonoscopy study conducted in United States got the prevalence between 25-40%. Generally, such prevalence is mostly affected by geographical factors and variation of local incidence rate of colorectal cancer. This condition supports the idea of environmental influence affecting development of colorectal adenoma.[1,3]

Age and gender also have role in developing colorectal adenoma. It is reported that elderly age and male are involved in development colorectal adenomatous. An autopsy study showed that 17% cases were found in subjects with age younger than 50 years, 35% cases were found in the age between 50-59 years, 56% cases were found in the age between 60-69 years and 63% in the age of 70 or older. Another study also showed that the incidence of colorectal adenoma in subjects with age of 70 or older has reached more than 50%.[1,2,3]

Colorectal adenoma usually has a small diameter (size < 1 cm), but it is commonly found in multiple form of adenomas. Increased age is strongly associated with the risk of multiple adenomas development. Colonoscopy and autopsy studies showed that colorectal adenoma was commonly found in distal part of colon and rectum, which has a similar distribution to colorectal cancer.[1,2,8]

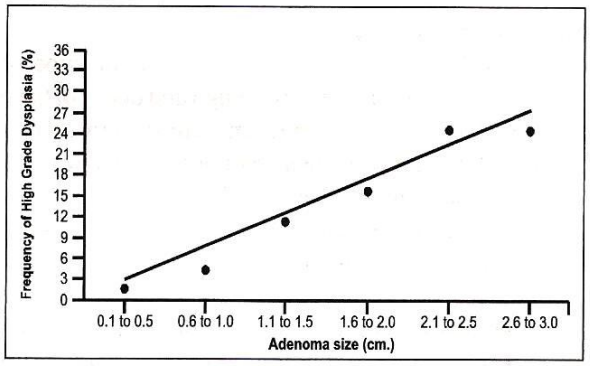

Figure 1. National polyps study: frequency of high-grade dyspepsia in adenomas by size[1]

Epithelial adenoma is one of preneoplastic group. Therefore, each of such adenoma own degree of dysplasia. Dysplasia itself is stratified into mild, medium and severe. Based on histological and clinical manifestation, adenoma is categorized into tubular adenoma (≥ 75% consist of tubular component), villous adenoma (≥ 75% villous component), tubulovillous adenoma (26-75% villous component) and flat adenoma which is a local dysplasia without any projection into lumen.[2,3,6,9]

Although these colorectal adenomas have potential capacity for being malignant, not all within this group progress into such transformation process. Large size of polyp, severe dysplasia, and villous histological pattern are associated with the increasing risk of its malignancy. National Polyp Study Workgroup

Table 1. Pathologic classification of colorectal polyps[1]

Neoplastic (adenomatous) polyps	Non-neoplastic polyps	Submucosal polyps
Benign	Hyperplasic	Lymphoid
Mild dysplasia	Mucosal	Lyphoma
Moderate dysplasia	Inflammatory	Other
High-grade dysplasia	Hamartomatous	
Severe dysplasia	Juvenile	
Carcinoma in situ	Peutz-Jeghers	
Malignant		
Invasive carcinoma		

introduced the concept of advanced pathological patterns become the risk of colorectal cancer development; i.e. adenomatous polyp with > 1 cm in diameter, high-grade dysplasia, > 25% villous pattern, and invasive cancer.[1,3,4,9]

Adenomas usually are asymptomatic and they are usually discovered at the time of colorectal cancer screening. A small adenoma unusually bleed, consequently the occult blood test frequently gives insensitive result. Positive results more likely to be obtained from occult blood test in pedunculated polyp, and it is also correlated to the size and its villous histological pattern. Symptoms like hematoschezia, abdominal pain with altered bowel habits are not specified for indicating appearances of adenoma.[1,3]

Non-neoplastic Polyps

Hyperplastic polyp is the most common type of non-neoplastic polyps, mostly benign and does not have potential capacity to become malignant. It is predominantly found in distal part of colon and rectum, with a smaller size (< 0.5 cm) and sessile. Considering its benign characteristic, further evaluation with colonoscopy or surveillance is not required even after its finding.[1,2,3,4]

Polyp mucous lining is usually thin and originated from normal mucosa of colon tissue. It is benign and can be found in colon or rectum and usually does not have any clinical significance.[2,3] Inflammatory colorectal polyps are commonly associated with severe colon inflammation. This condition is generated by severe and recurrent ulceration and regeneration (injury repair) in colon segment and rectum. It also associated with other inflammatory condition such as Inflammatory Bowel Disease (IBD), amoebic colitis, ischemic colitis, schistosomiasis, dysentri, and sometimes without any underlying inflammatory process. Inflammatory polyp may have a large and solitaire size, so that it may cause abdominal pain and obstruction.[1,2,3,5,6]

Hamartomatous polyps are divided into juvenile polyp and Peutz-Jegher polyp. Juvenile polyps usually appear as solid rectal polyps in children less than 20 years of age or occasionally it may appear in adolescence. Most of them are pedunculated with red and smooth surface, and approximately 90% of cases appear with symptom of rectal bleeding (hematoschezia). Some cases may be followed by abdominal pain and prolapsed of polyp out of the rectum.[1,2]

Peutz-Jegher polyps are a non-neoplastic hamartomatous polyp which may occur in any part of gastrointestinal tract, from the stomach to rectum. It is usually associated with polyposes hereditary syndrome, but it may also found sporadically. It usually has a large size (> 3 cm) and it may reach 5 cm.[1,3,5] Lymphoid polyp is a benign submucosal polyp which may occur due to hyperplasia of normal lymphoid tissue at the mucosa or submucosa of gastrointestinal tract. It is a result of lamina propria expansion caused by lymphocytic infiltration. It is usually solitaire, appears in rectal area, and has a small size[1,2]

Lyphoma is commonly found at proximal part of colon or around the ileocaecal. Generally, it is solitaire, asymptomatic, and often discovered by chance in colonoscopy. Asymptomatic colon lyphoma usually does not require any further treatment or evaluation[1,2] Familial Adenomatous Polyposis (FAP) is one of genetic disorder characterized by progressive growth of multiple (hundreds to thousands) colorectal adenoma. The prevalence of FAP is approximately 1% of all colorectal cancer cases. The suffered patients are suspected to have deficiency in APC gene at the long arm of chromosome 5. Adenoma usually occurs at the first or second decade of life. In the untreated patients, colorectal cancer may occur in fourth or fifth decade of life. Gardner's syndrome is a variant of FAP, characterized by adenoma and extra intestinal involvement.[1,10]

Juvenile polyposis syndrome is a multiple gastrointestinal juvenile polyp, which has familial characteristic and approximately occurs in 25% of families. Familial involvement may be limited on stomach and colon, or it may become extensive from stomach to rectum. The clinical manifestation may include anemia, abdominal pain, rectal bleeding or recurrent intussusceptions. Sometimes, extra intestinal congenital disorders are also found to be involved. Patients with such familial syndrome may have a risk in the future likelihood of developing colon cancer and they are recommended to have colonoscopy/endoscopy surveillance to remove the polyp.[1,10]

Peutz-Jegher's syndrome is characterized by multiple hamartomatous polyps and mucocutaneus melanin pigmentation. The polyps usually involves small intestine with total number of polyp less than 100. Discourage feelings usually occurs in second or third decade of life with main symptoms of gastrointestinal obstruction. Patients with Peutz-Jegher's syndrome have risks of developing gastrointestinal malignancy caused by the transformation process into adenoma. Therefore, it is strongly recommended to perform endoscopy surveillance of upper and lower gastro-intestinal tract, followed by polyps removal.[1,2,7,8]

Hereditary Non Polyposis Colorectal Cancer (HNPCC) is characterized by the growth of some colorectal adenoma with increasing risk of colorectal cancer. Adenomatous polyps in HNPCC are predominantly found in proximal colon and it may be related to possible development of extra-colon malignancy. Considering the high risk of being

malignant, periodic endoscopic surveillance for gastrointestinal tract is highly recommended for every 1-2 years in patients with confirmed HNPCC.[1,2,8]

GASTROINTESTINAL TRACT MALIGNANCY

Colorectal Cancer

Colorectal cancer is one the most common cause of death and morbidity in US and other Western countries. It is estimated that 135,000 new colorectal cancer cases were found in US in 2001, and it was related to 57,000 deaths which were associated with cancer. Cancer growths in a long period of time as a result of predisposed genetic and environmental factor. Therefore, early detection and early removal of preneoplastic initial lesion will increase the survival rate.[4,11]

Colorectal cancer occurs through a complex interaction between affecting genetic and environmental factors. The roles of genetic factors are usually affected by hereditary syndrome (such as FAP and HNPCC); while spontaneous cancers are mostly affected by environment factors such as repeated exposure of carcinogenic condition or environment. In the both aforementioned conditions, the cancers do not occur spontaneously but it rather develops through a progressive process by altering mucosa of colon (dysplasia, adenoma, etc).[4,11]

Many evidences showed the role of environmental factors in developing gastrointestinal tract malignancy. The prevalence of colorectal cancer itself extremely varied, from the higher incidence in North America, Western Europe, Australia to the lower such as in Asia, South America and Africa. The environmental factors are categorized into protective factors (high fiber diets, aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) consumption, diet containing carotene, calcium intake, physical exercise, etc), and carcinogenic factors (low-fiber and high-fat diets, alcohol, smoking, obesity, etc). The risk of colorectal cancer development itself will increase in line with the increasing of age.[4,11,12]

Individuals who have hereditary disorder such as FAP and HNPCC are identified as a group of persons who were born with susceptible genetic (hereditary) of colorectal cancer. In addition, the non-hereditary colorectal cancer (sporadic) also has still been influenced by genetic factors. In the last group, multiple mutation influenced by environmental factors become a trigger for developing colorectal cancer. Genetic alteration that may induce the development of colorectal cancer can be divided into: increased proto-oncogene, loss of tumor suppressor gene activity and abnormal gene involved in the process of DNA repair.[1,4,11,13]

The Role of Colorectal Polyp in Colorectal Cancer

Most of colorectal cancers in the population are actually originated from adenomatous polyps. All adenoma have dysplastic epithelial cells which are usually benign. However, they may also have potential capacity to develop malignant degeneration.

This transformation into malignant degeneration has been known as the adeno-carcinoma sequence. Usually, the transformation in sporadic adenoma lasts within a quite long period of time (5-15 years) which is different from other hereditary disorder that may occur in a shorter period.[1,2,13]

Adenomatous polyps are related to abnormal cell proliferation, which acts as a basic process of neoplasia. This kind of abnormality arise with a complex process related to changes of genetic factors and may induce the imbalances including increased proto-oncogene (K-race), loss of tumor suppressor gene activity (APC, p53) and abnormality in DNA repair related gene (hMSH2, hMLH1, etc).[1,4,11,13]

The risk of evolution from adenoma into carcinoma is tightly associated with the size of polyp and its histological characteristics. A large polyp with high proportion in villous architecture is more likely to be carcinogenic. The same possibilities also come with polyp containing a larger number of distortion architecture and atypical cells (moderate to severe dysplasia). A large polyp usually contains more villous architecture and dysplasia.[2,3,6,7]

DIAGNOSIS AND MANAGEMENT

Detection and Diagnosis

Although the colorectal adenomatous polyps may cause an occult bleeding; but it is usually asymptomatic. The process of adeno-carcinoma sequence into colon and rectal malignancy develops slow and takes a long time before the symptoms occur. Consequently, polyp is one of pre-malignant lesion that hardly detected and it is usually discovered by screening for colorectal cancer. Occasionally, progressive polyp development may cause colorectal cancer-like symptoms, starting from abdominal pain to hematoschezia.[1,6,12,14]

Table 2. Factors determining risk of malignant transformation within colonic adenomuos polyps[13]

High risk	Low risk
Large size (especially > 1.5 cm)	Small size (especially < 1.0 cm)
Sessile or flat	Pedunculated
Severe dysplasia	Mild dysplasia
Presence of squamous metaplasia	No metaplastic areas
Villous architecture	Tubular architecture
Polyposis syndrome (multiple polyps)	Single polyp

Screening assessment to find the pre-cancer polyp or early stage of colorectal cancer in asymptomatic patients has become main effort to decrease mortality and enhance survivals. There are some methods of examination to detect colorectal polyp but not all of them may provide satisfying result in establishing the diagnosis. Accurate selection of diagnostic methods by considering cost-effectiveness principles may bring easier process in making diagnosis and organizing further management.

Occult Blood Test

This test is so simple, easy and cheap that some countries recommend it as a screening method for colorectal lesion (polyp/malignancy). However, this test has some weakness, i.e. due to its less sensitivity and low specificity, and negative results obtained from this test cannot exclude the possibility of such lesion. In general, polyp with a size < 1 cm does not cause any bleeding. Therefore, there are only approximately 20-40% patients with polyp who have positive results in blood occult test.[1,12,14,15,16]

Barium Enema

Polyp can also be detected by performing radiological test (called barium enema), but it has limitations for small-sized polyps and it is not able to obtain biopsy tissue. The advantage of this test is due to its non-invasive characteristic. When it is used together with positive-result of occult blood test, it may have increased sensitivity up to 58%.[4,12,15]

Rectal Sigmoidoscopy

A number of studies indicated a significant decrease of mortality rate in a group that sigmoidoscopy examination, although it is only limited to the examined part of colon. Most polyps are discovered at the areas where it is easily reached by colonoscopy considering its predilection, and when there is any polyp found, some experts will suggest colonoscopy procedure to find other possible lesion at more proximal part of the colon. Flexible sigmoidoscopy is more efficient than the rigid in establishing the diagnosis of colorectal polyp. Due to its limitations, simultaneous use with the occult blood test or barium enema may increase its specificity and sensitivity.[9,12,15]

Colonoscopy

Until now, this test has still become a gold standard for detecting polyps in colon area. It is superior compare to other kind of tests because its capability in obtaining biopsy tissue and may provide therapeutic intervention in a time. But, considering its potential capability of being malignant, all polyps found in gastrointestinal tract by radiological examination must undergo histopathological examination to assure the possibility of malignancy occurrence.

A part from its histological description, the macroscopic features of colonoscopy may also helpful in recognizing the type of possible polyps. For example, tubular adenoma has more red color in appearance than its adjacent tissues and it has a smooth surface; while villous adenoma usually appears larger with a sessile, frondlike, rough and soft appearance. In contrast, simple mucosa polyp usually looks small with an appearance similar to the surrounding normal mucosa. Hyperplastic polyp is usually small, sessile and pale; whereas inflammatory polyp is usually found large, solitaire with inflammation signs and ulceration.[2,15,17]

The available studies indicated that colonoscopy has sensitivity up to ± 96%. However, some other studies demonstrated some of its shortcomings that in some cases with small-sized polyps (< 10 mm) were missed in colonoscopy examination. Moreover, it is also strongly affected by the operator's skill, preparation prior to the test, cost and its invasive characteristic.[2,14,15,18]

The advanced progress of various colonoscopy techniques may enhance its specificity in detecting colon lesion. Chromoscopy and magnifying colonoscopy may assist further in clarifying the image of gastro-intestinal mucosa. Therefore, those methods may increase the ability of detecting small-sized polyps or flat-type polyps. Kato et al, demonstrated that such technique has 98% sensitivity and 92% specificity to distinguish the neoplastic/invasive with non-neoplastic/non-invasive lesions. Endoscopic Ultrasonography (EUS) may be also performed to improve ability of detecting suspected lesion with possible gastro-intestinal malignancy.[12,14,17,18,19]

Virtual Colonoscopy

Virtual colonoscopy or CT colonography is a non-invasive imaging method test that recently has developed fast as a diagnostic method for colorectal polyp. Some studies showed satisfaction in the results compare to the gold standard examination, colonoscopy, especially for lesion larger than 10 mm. The drawback of this test is the inability to get histopathological result and inaccuracy for the small-sized polyp (< 10 mm). Pickhardt et al, arranged a comparison study between conventional and virtual colonoscopy with the result as seen in the following table.[14,20,21,22]

Table 3. Sensitivity and specificity of virtual colonoscopy[15]

Polyp diameter (mm)	Sensitivity of		Specificity of virtual colonoscopy (%)
	virtual colonoscopy (%)	optical colonoscopy (%)	
≥ 10	93.8	87.5	96
8	93.9	91.5	92.2
6	88.7	92.3	79.6

TREATMENT

The treatment of colorectal polyp is generally divided into surgical and non-surgical management. By the advance technology in endoscopy, many

patients have been kept away from surgical treatment of colorectal polyp and such technology may also minimize possible risks. This method has become the treatment of choice due to its low complication.[2,3,23]

Polypectomy colonoscopy is an alternative treatment for colorectal polyp removal. It is usually done by using snare polypectomy, hot forceps biopsy and excision biopsy. Snare polypectomy is usually performed in pedunculated polyp, and for the small sessile type polyp may be treated by hot forceps biopsy or excision biopsy. Other technique that may also be performed is Endoscopic Mucosal Resection (EMR), a polypectomy by using saline injection (saline assisted polypectomy).[1,2,9,24,25]

Argon plasma coagulation and laser ablation are other alternatives to eliminate a large number of small polyps that commonly found in hereditary disorder (FAP, HNPCC, etc), and large-sized sessile polyps with residues. This procedure is effective, fast and relatively safe if carried out by experienced expert. Polypectomy colonoscopy is relatively safe with low complication. Some post polypectomy complications that may occur are perforation and bleeding.[9,17,24,25]

Recently, surgical treatment to remove polyps has become the last choice after all colonoscopy procedures have been tried and only performed if there is malignancy features that have reached the root of polyp or there is no firm boundary seen within normal and malignant area. This action is carried out to remove possibilities of regional metastases and tumor residue. Surgical treatment may also be performed if polyp removal can not be done by colonoscopy (large-sized sessile polyp) or if there is a doubt whether the polyp that has been fully removed by colonoscopy has histological features that show a poor differentiation of adenocarcinoma. Surgical treatment to remove polyp in hereditary polyp disorder (FAP, etc) should be considered regarding its high risk in developing the gastrointestinal malignancy.[1,2,3]

EVALUATION AND PREVENTION

Further evaluation following elimination treatment of polyps takes an important role in preventing the development of gastrointestinal malignancy. Particularly, neoplastic polyp acts as a precursor of lesion for malignancy. Therefore, post-polypectomy surveillance must become a part of treatment management. After polyp elimination by polipectomy is carried out, it is recommended to perform colonoscopy surveillance in the interval of 3 to 5 years period following the treatment, depends on results that might be found. In some case, such as patients with large-sized sessile polyp (> 2 cm) who have successfully undergone excision colonoscopy, it is recommended to be followed up at the third and sixth month. Similar suggestion is also recommended for patients with genetic and hereditary disorders (FAP, HNPCC), i.e. to have earlier screening and evaluation.[1,3,9,26]

For the group with colorectal adenomatous polyps who have already undergone polyp elimination, a prevention effort of recurrence and malignancy development has been incorporated as part of inseparable treatment management. Life style changes such as low-fat and high-fiber diet, maintaining ideal body weight, avoiding smoking and alcohol consumption are some efforts to modify the risk factors.[3,9,11,26]

Some studies demonstrated some benefits of consuming NSAIDs and calcium carbonate to prevent recurrent adenoma and to inhibit the process of adeno-carcinoma sequence. There are two mechanisms assumed to play a role as anti-carcinogenesis in NSAIDs, i.e. by inducing the apoptosis process and inhibiting the cyclooxigenase enzymes which are important in prostaglandin synthesis. A number of studies showed that prostaglandin has a role in tumor angiogenesis, cell proliferation and apoptosis inhibition. Some preliminary studies indicated some advantages of either conventional NSAIDs consumption (aspirin) or the selective NSAIDs such as the class of COX-2 inhibitor.[2,11,27,28]

CONCLUSION

Colorectal polyps, particularly the adenomatous polyps, are a precursor of lesion which has an important role in developing gastrointestinal tract malignancy. Adenocarcinoma sequence is a long process and often asymptomatic so that it is frequently missed and resulting in increased morbidity of gastrointestinal tract malignancy, especially the colorectal cancer. Early detection and elimination of such precursor of lesion are very important in decreasing the incidence of colorectal cancer.

Early evaluation in colorectal cancer risk group is a strategy to detect lesions of early malignancy; while further evaluation and prevention measurements are inseparable parts of colorectal polyp in treatment management to avoid the development of colorectal polyps.

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