Diagnosis, Management and Prevention of Colon Polyps

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ABSTRACT

Colon polyps can be a predisposing factor for colon cancer; they should be immediately removed once they are found. Most of colon cancer arises from adenoma. Most adenoma cases are asymptomatic. It is frequently detected at the first time when someone undergoes screening for colorectal cancer with the imaging modalities in the medical check-up. Approximately, 10-40% of patients without any symptoms with the positive result of occult blood test suffer from adenoma. By using colonoscopy, we can detect for adenoma cancer and adenoma polyps, so colonoscopic procedure is recommended for individuals with the high risk for colorectal cancer. Excision and polyp removal during colonoscopy is a treatment choice to lower the risk for developing colon cancer. Surgical intervention is usually required in the management of adenoma polyps for those with an extremely large size which cannot be resected through endoscopy. There are some suggestions for preventing of adenoma growing such as vegetable and fruit diet, limit intake of meat and fatty food. And finally do physical activities regularly and stay away from alcohol and cigarettes

Keywords: *colon polyps, colonoscopy, polypectomi, vegetable and fruit diet*

INTRODUCTION

The term colon polyp, is used to describe any protrusion arising on the mucosal surface into the colon lumen. Polyps grow slowly, a small quantity of them have a risk for malignancy (< 1%). However, polyps have the high prevalence in population (especially with growing age), so it is very crucial that they should be immediately removed once they are found because they can be a predisposing factor for colon cancer.[1]

Roughly, polyps can be categorized into neoplasms and non-neoplasm. Then, neoplasmic polyps can be divided into adenomatosa (pre-malignancy) and malignancy. Approximately 95% of the total number of colon cancer arises from adenoma. It is estimated that approximately 60% of the total number of polyps removed by colonoscopy are adenomas.[1,2]

The risk for adenoma to develop malignancy in the future is correlated with the macroscopic appearance of polyps (size, shape and site) and the microscopic appearance of the anatomical structure and the degree of dysplasia. These findings are used by clinicians to predict the potential of a polyp to develop malignancy and serve as the therapeutic guidances and as a further observation.[2]

Patients with polyps usually do not have any symptoms so that early diagnosis cannot always be established. In this paper, the diagnosis, the most important therapy to prevent the incidence of polyps in order to inhibit the course of disease into malignancy will be addressed.

PATHOPHYSIOLOGY

The epithelium of colon mucosa are *self renewal*, organized and in balance between proliferation of cells at the base of crypti, and maturation of colonocytes that will move upward on to the crypti and cell apoptosis occurs on the upper part of crypti. This process requires 3 until 6 days.[1,3]

The typical characteristic of adenomatosa cells is the loss of control over normal growth. These cells will keep on proliferating and after they reach the upper part of crypti, they do not exit into the colon lumen. These cells even get abundant and eventually return to the area of normal mucosa, triggering the response of mesenchyme tissue that will establish the architecture of adenoma microscopically.[2-4]

The growth rate from adenoma to be malignancy is quite various; it generally takes between 5 and 10 years. Patients with inherited disease such as familial adenomatous polyposis (FAP) or other hereditary diseases such as hereditary non polyposis colorectal cancer (HNPCC) will have a faster rate of tumor growth in forming adenoma and it tends to be malignant.[1,3,4,5]

Table 1. Prevalence of Colorectal Polyps[2]

Population	Prevalence of adenoma (%, ~ - age 50)
Japanese (Hawaii)	65
Negroid (New Orleans)	40
Negroid (South Africa)	30
Sweden (Trellabang)	30
Japanese (Akita)	30
Spanish (Barcelona)	20
Brazilians	15
Swedish (Bolinas)	10
Japanese (Miyago)	10
Colombian (Cali)	5
Costarican	5
Irani	< 5
Bolivian	< 5

PREVALENCE AND RISK FACTORS

Prevalence

In the United States, based on the results of colonoscopy and autopsy, the prevalence of adenomatous polyps is around 40 - 50% and increases in population aged 50 -60 years. Geographic conditions also influence the variety of prevalences, for example, two different ethnic groups: from the homogenous group in Japan, it was found that there is 20% difference in prevalence of adenomatous polyps in the population aged 50 years.[1,2,5]

Morbidity and mortality

Adenoma infrequently causes massive haemorrhage or colon obstruction. The morbidity and mortality are correlated with the carcinoma that is originated from an adenoma. A national multi-centre study has revealed that early detection and removal of adenomatous polyps can lower the incidence of colorectal cancer.

Risk factors

- Race

  The risk for adenoma substantially varies among different populations. The difference in race does not constitute an independent determining factor. Eating habit and environment factor play is important in explaining the differences that happen all over the world. Japanese who live in Hawaii have a high prevalence for adenoma compared with Japanese who live in their country, Japan. This is also valid for the black people who live in New Orleans, they have a higher risk for adenoma than black people who live in South Africa.[1,2]

- Gender

  Some investigators have found that prevalence of adenomatous polyps is around 30% higher in men than in women.[2]

- Age

  The prevalence of adenoma increases with age. Adenoma is seldom found below 30 years of age, except for those who have siblings/relatives who have the history of FAP. Most trials have shown that the prevalence of adenoma starts to increase at 40-50 years of age and continues to rise until 80 years of age.[1,2,4,5]

- Genetic factor

  Genetic susceptibility: there are 2 dominant autosomal types which can be passed on in the incidence of adenomatous polyp that comprises of around 3% of the cases, among others:

  - FAP which is caused by germinal mutation of APC gene. The characteristics finding is the identification of hundreds up to thousands of adenomatous polyps on the colon in the adolescence period (approximately aged 15 years) and almost 100% of them run the risk for colorectal cancer at the age of 40 years if the polyps are not well treated. In the incidence of adenoma or carcinoma, it is presumed that the genetic process has a role in the formation of excessive mutations and expansion of a clonal cell. At the beginning of mutation, it frequently involves inactivation of adenomatous polyposis coli (APC) gene, a gene suppressor tumor. Mutation at APC gene can cause cell proliferation uncontrollable so that FAP occurs. Mutation of somatic APC-gene occurs in approximately 80% in adenoma cases.[3-5]

- HNPCC is caused by germinal mutation at several repair genes DNA (MSM2, MLH1 and MSH6). Only some of the cases progress to be adenomatous polyp. However, the speed of progression to be colorectal cancer is very high. Progressive mutation that occurs at the adenoma cells includes activation of oncogenes (ki-ras) and inactivation of tumor suppressor genes (TP53) and DNA repair genes such as MSH2, MLH1. In some individuals, mutation causes a clonal cell to have a higher half-life than that of the surrounding cells. Mutation of the next cycle and clonal expansion cause the appearance of an adenoma, higher degree of dysplasia and it is invasive as well as metastatic like the common nature of carcinoma.[5-8] Cancer at HNPCC can occur at young ages-approximately at 40 years of age and generally occurs to proximal colon (60-70% proximal flexura lienalis) and it is seldom metastatic. In addition to it, the incidence of adenoma can occur at polyposis haematoma even though it is very rare. It is a dominant autosom in Peutz Jeghers syndrome and familial juvenile polyposis that usually involves small intestines.

- Family history

  Every patient with the family history of adenoma or colorectal cancer has higher susceptibility to adenoma-around 1½ - 2 folds.[1,5]

- Diet

  Obesity, lack of physical activity, high-calorie and fat diet, low-fibre diet and high-meat diet are correlated with the increasing risk for adenoma and colorectal cancer. Alcoholism and smoking have been said to increase the risk.[9]

SIGNS AND SYMPTOMS

Most adenoma cases are asymptomatic. A report from 800 hospitals shows that 32% of hospitalized patients with colorectal polyp did not have any symptoms.[10] It is frequently detected at the first time when someone undergoes screening for colorectal cancer with the imaging modalities in the medical check-up. Other symptoms frequently found usually indicating larger adenoma (more than 1 cm) include grossly or occult rectal haemorrhage, change in bowel habits, abdominal pain, rectal prolapsed, obstruction of the intestinal, intussusceptions and diarrhea.[11]

In the cases of FAP, despite the high number of polyps, hundreds or even thousands, the symptoms are generally detected late or found when it has progressed to colorectal carcinoma. The histological observation reveals, unlike cancer, in which there are ulcers on the surface that cause bleeding, they are seldom found in adenoma.[12]

Physical examination

Large polyps can sometimes be detected by performing "rectal toucher"

Table 2. Recurrence of adenoma > 9 mm in the second and fourth years in the Australian Polyp Prevention Project[9]

Intervention		Adenoma (1 cm) Recurrence			
		2nd years		4th years	
Oats	Low fats	No	Yes	No	Yes
No	No	93	6	74	6
	Yes	93	5	72	4
Yes	No	89	7	66	7
	Yes	97	0*	75	0*

* Significant reduction ($p < 0.03$) compared with the group that consumed high-fat diet or without addition of oats. The results were seen in the randomly selected subjects in the low-fat intervention with/without oats intervention.

Table 3. Anatomical Distribution of Colorectal Adenoma[1]

Examination	Ascenden (%)	Transversum (%)	Descenden (%)	Sigmoid (%)	Rectum (%)
Colonoscopy	10	10	30	45	5
Autopsy (all adenomas)	30	20	15	15	20
Autopsy (adenoma > 1cm)	15	15	25	35	10

Histological classification of polyps.[1,4]

Adenoma is classified based on size, morphology and degree of dysplasia

- Size: most adenomas are small (< 1 cm). Large adenomas (> 1 cm) tend to indicate severe dysplasia and bad architecture and potential risk for malignancy.
- Morphology: adenoma is traditionally described as tubular, tubulovilosa and villous based on the presentation of vilosa components in a polyp.

  Tubular adenoma has components of villous tissue, around 0-25%. Approximately 70-80% of the total adenomatous polyps are tubular. The size tends to be smaller than the size of villous adenoma. It is rather dark red in colour compared with the colour of the surrounding mucosa and the surface is smooth even though in some cases it is granulated. Frequently, the erosion and ulceration on the surface are found even though the frequency is lower than that of carcinoma.

  Tubulovilosa adenoma contains approximately 25-75% of villous tissue. The frequency is around 10-25% of the total adenomas and the size is usually moderate (between the type of the tubular size and villous adenoma).

  Vilosa adenoma contains more than 75% vilosa tissue. The frequency is around 5% of the total adenomas. It tends to be larger in size and has the higher potential to be malignant. It often affects patients of above 60 years of age. The common shape is sessile which tends to be located at the distal part of the colon.
- Degree of dysplasia

  Dysplasia is a change toward malignancy, histologically. All adenomas constitute dysplasia that reveals the degree of hyperchromation, prominent nucleus, pleomorphic nucleus, and increasing mitosis. Dysplasia is categorized into the low and high degrees. Carcinoma is differentiated from dysplasia with the presence of invasion of neoplasmic tissue on the muscular mucosa layer. Low-degree dysplasia is characterized by basal nucleus, irregular glands and small amounts of goblet cell and mucin. High degree dysplasia is characterized by the loss of the architecture of the glands and increasing mitosis.

SUPPORTING EXAMINATION

Laboratory examination

Examination of occult blood in the faeces is conducted to detect the possibility of haemorrhage in a big adenoma. Approximately, 10-40% of patients without any symptoms with the positive result of occult blood test suffer from adenoma, depending on the patient's age.

A new technique has been found to defect the presence of blood in the faeces based on the immunological reaction – this technique will be available in the short time and it is expected to increase the specificity of the examination.

Other examinations

CT scan and Magnetic Resonance Imaging (MRI), virtual colonoscopy have still been investigated to detect the presence of adenoma or carcinoma on the colon. So far, virtual colonoscopy has still been less sensitive than colonoscopy in detecting adenoma with the size < 1 cm and runs possibility of high false positive. However, the rapid progression of technology in this era has been expected to increase the capability of this modality.

Flexible sigmoidoscopy has been recommended for those who run the high risk for adenoma or colorectal cancer. Flexible sigmoidoscopy can delineate the left side of the colon around the half part of the adenoma and cancer is located on that side (10% at the rectum and 35-45% at the sigmoid). Flexible sigmoidoscopy can be inserted into the 48-55 cm depth of the anus.[13] Perforation as the complication of sigmoidoscopy is very rare approximately in one out of 10,000 procedures.[14] If malignancy is spotted during sigmoidoscopy, it is recommended further proceeding with total colonoscopy because the possibility of malignancy in other sites can not be readily excluded. Sigmoidoscopy is easier to be conducted and more cost-effective than colonoscopy. Screening with flexible sigmoidoscopy in population over 50 years of age will lower the mortality by 40-50%.

Colonoscopic screening for adenoma cancer and adenomatous polyps is recommended for individuals with the high risk for colorectal cancer. Several trials have shown that the relative first-generation screening in patients of above 55 years of age is an effective tool for detecting colorectal abnormalities.[15] Enthusiasm among people in terms of colonoscopic screening has been rising lately. Visualization of the whole colons by colonoscopy routinely as well as removal of polyps will lower the mortality rate by more than 80%. Colonoscopy is safe to be performed on adults and children.[16] Biopsy or polipectomy in all polypoid lessions is important for

histological analysis. To be noteworthy, good cooperation between gastroenterologists, anatomy pathologists and radiologists is required differentiate specimens in accordance with the site of the polyp taken during biopsy.[17]

Therapy

Excision and polyp removal during colonoscopy is a treatment choice to lower the risk for developing colon cancer. Several techniques for removing polyps which have been well known include forceps biopsy and excision by using a snare (with or without an electric cauther). Polypectomy with colonoscopy is one of the choice procedures for treatment of adenomatous polyps and colonoscopy is usually recommended being performed regularly for patients who have previously undergone removal of polyps. The National Polyp Study has shown that a survey on regular colonoscopy with polypectomy could reduce the incidence of colorectal cancer by 76%-90%.

Practically, all polyps should be removed. Polyps with the size of less than 5 mm are usually benign and seldom cause bleeding. Polypectomy without an electric cauther (cold snare) is quite effective for small-sized polyps. Large polyps sometimes encountered more than 2 cm are usually adenomatous and should be removed in toto if they are pedunculated. If they are sessile, they should be gradually removed (piece meal).[18] The number of polyps which can be removed safely depends and the size. For FAP patients, colectomy instead of polypectomy is an indication.[19]

Pharmacotherapy

Sullindac (clinoril) is an anti-inflammatory non-steroid agent (NSAID). On this medication, is showed that the number and size of polyps decreased in patients with FAP, but it is still controversial. Mechanisms of NSAID to reduce the number of polyps have still not been understood, but it is postulated that it involves the selective apoptosis induction of cells that die in the adenoma mucosa. Sullindac is a sulfoxid that metabolizes the anti-inflammation sulphide and sulfon in which these two metabolites have affinity to apoptosis cells of the colon epithelia. The recommended dose is 150-200 mg twice daily.[20] Celecoxib (celebrex) especially inhibits the activity of COX-2. The recommended dose is 400 mg orally, twice daily.[21,22] Aspirin, some trials and cohorts have showed that administration of Aspirin is correlated with the declining mortality rate caused by colon cancer, but the mechanism has not been elucidated yet.[23,24]

Surgery

Surgical intervention is usually not required in the management of adenomatous polyps except for those with an extremely large size which cannot be resected through endoscopy. If the site of the adoma is in close of the anus, transanal resection can be performed. If the position is rather proximal laparoscopy or laparotomy will be required with segmental colon resection and evaluation of the enlargement of the lymph node.

Table 4. Recommendation of Screening in Accordance with *American Cancer Society*

Colon and rectum	M/F; age 50 + (screening should be initiated or more frequently in people who have the family history for or adenoma polyps, chronic IBD and FAP and HNPCC)	(A) Fecal occult blood examination test (FOBT)	Annually, in addition to FOBT, sigmoidoscopy is recommended
		or	
		(B) Flexible sigmoidoscopy	Every 5 years; in addition to flexible sigmoidoscopy, FOBT is conducted
		or	
		(A) and (B)	Highly recommended by American Cancer Society
		or	
		Double-contrast barium enema	Every 5 years
		or	
		Colonoscopy	Every 10 years

Prevention

- Diet
  Epidemiologic observation has obtained several food factors that are potential for the prevention of adenoma, among others, vegetables and fruit. Red, yellow, orange and green fruit and vegetables such as orange, strawberries and carrots are rich in complex substance-usually called antioxidants. Uncooked vegetables such as cabbage, Brussels cabbage, and broccoli contain chemical substances that are very potent to fight cancer. Antioxidant supplementation such as vitamins C and E have not been proven to have a beneficial effect.[9,25]
- Folic-acid
  In 1999, a trial that involved a big number of nurses was published. It was observed for 14 years. Folic acid was protective in those subjects that received folic acid as much as 400 micrograms daily derived from food or vitamins. They found that it had the nature of preventing the incidence of colon cancer.[28]
- Meat and saturated fat
  Meat and saturated fat in ice cream and food will reduce the amount of digestive enzymes and gall fluid. Some of these products have been said to cause cancer in trial animals. There has been evidence that high consumption of meat and saturated fat contained in food has the bad potential role for colon health.[25,26]
- Fiber
  The trials in the years 1960 and 1970 revealed a correlation between high-fiber diets with the colon-cancer cases in the mountainous areas of Africa. A lot of subsequent trials showed a positive beneficial outcome for health so that high-fiber diet is highly recommended.
- Calcium
  Calcium is one of the most abundant minerals in the body. It is required for the formation of bones and for the necessary chemical process in the body such as regulation of cell growth. Supplementation of 1-1,5 grams of carbonate calcium daily is recommended to reduce the incidence of recurrent polyps by 24% in patients who have previously undergone polyp resection
- Activity
  A lot of epidemiological research has postulated that regular physical activity will result in a protective effect against colon cancer.

CONCLUSIONS

1. Polyps should be immediately removed if encountered, especially if they are adenoma.
2. Vegetable and fruit diet that is rich in fiber is highly recommended. Limit intake of meat and fatty food.
3. Do physical activities regularly and stay away from alcohol and cigarettes.

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