

Skin Tags – A Marker For Colon Polyps?

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Abstract: The frequency of colorectal cancer increased during the first half of the twentieth century, but for the last four decades, it appears to have stabilized. Today, the average American has a 5 percent probability of developing colorectal cancer during a 70-year life span. The majority of cases occur in persons aged > 50 years; the incidence increases up to age 75 years, after which there is a decline. Etiology is unknown; however, environment, genetics, and carcinogens have been implicated. Genetic relations of skin tags, colon polyps, and colon cancer are a matter of ongoing research. If such relations could be established, it could provide clinicians with a possible additional marker for persons at increased risk of colorectal adenoma and adenocarcinoma. Two cases are presented with a brief review of the literature. (J Am Board Fam Pract 1990; 3:175-80.)

Cancer of the colon and rectum is one of the most common malignancies of the internal organs encountered in both men and women. Each year in the United States, there are approximately 150,000 new cases and 60,000 deaths.¹⁻⁵ The worldwide incidence is estimated at approximately 500,000 new cases annually.^{3,4,6} The survival rate at 5 years for all stages of the disease is about 40 percent.⁵ The prognosis of colorectal cancer is definitely related to its depth of penetration through the bowel wall and the amount of involvement of lymph nodes. It is a problem of great magnitude and worthy of all possible efforts to improve these grim figures. It is because of these facts that identification of high-risk persons at the primary care level is of great importance.¹⁻⁹

One of the most practical and desirable means of dealing with colorectal cancer would be to identify these persons at highest risk and to provide appropriate intervention during the premalignant or earliest stages of the disease. It has been shown that, when colorectal cancer is detected in the asymptomatic stage, almost all patients have localized and, therefore, potentially curable disease, with the 5-year survival rate improving to about 90 percent.⁴ The concept that adenomatous polyps and villous adenomas are precursors of colorectal adenocarcinoma has been essentially accepted universally, and there is a

wealth of supporting evidence in the medical literature.^{1-3,5,7,8} Our current diagnostic capabilities, including flexible sigmoidoscopy, colonoscopy, and single and double contrast barium enema radiographic studies, provide us with highly specific and sensitive means for both visualizing and then excising these premalignant lesions, usually on an outpatient basis.^{2,6,9}

Skin tags, also called acrochordons, are skin appendages of various shapes and sizes occurring on any part of the body, but they are most often found in the axilla, neck, or groin. They are usually at least 2 mm long, 2 mm in diameter, and often hyperpigmented.

As association between skin tags and colonic polyps in patients with acromegaly has been reported,¹⁰ but the simultaneous presence of skin tags with colonic polyps in otherwise normal persons has been a subject of interest and research, especially their genetic relations. In order to prove scientifically these relations, blood samples of members of family trees with skin tags, colon polyps, and cancer would need to be studied using DNA probes. These, however, are still under development and will not be available to clinicians in the foreseeable future. Skin tags could serve as a means of identifying patients at a greater risk for having colon polyps, which sometimes are precursors of colon cancer. Because present available methods of cancer prevention are limited, reliance has to be placed on secondary prevention and early detection. The emphasis in primary care is screening, but special emphasis on skin tags alone is not warranted because they are not yet a scientifically validated risk factor.

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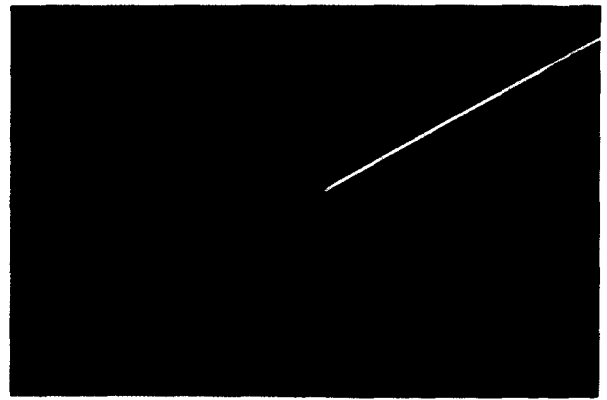


Figure 1. Skin tags: markers for colon polyps. Left: colon polyp. Right: skin tag.

Two cases are presented with a brief review of available literature.

Case 1

A 51-year-old white woman was seen for a routine physical examination. She had a typical acrochordon in the left inguinal area, as well as a very large pedunculated skin tumor on the left proximal, posterior thigh, measuring 2 cm × 3 cm, which she stated had been first noted about 2 years previously. It had steadily become larger, and she requested its removal. She also had a heme-positive stool on rectal examination, but she had no other colorectal risk factors except for her age. Her family history was negative for colorectal cancer. With a flexible sigmoidoscope, three polyps were identified at 30 cm, 40 cm, and 50 cm. They ranged in size from 1 to 2 cm. Full colonoscopy for definitive intervention was then arranged (Figure 1).

Case 2

The patient was a 72-year-old white woman who was seen for a routine physical examination. She had a healthy life style and a negative family history for colorectal cancer. Three skin tags were identified, but the remainder of the examination was normal. A screening flexible sigmoidoscopy a few days later showed two polyps located 15 cm and 25 cm from the anal verge. The patient was referred for colonoscopy, and another large villous polyp was detected at 75 cm.

Discussion

There have been a number of studies investigating the possible association of simple skin tags

(acrochordons) with colorectal polyps, thus providing a possible additional marker for increased risk of colorectal adenoma and adenocarcinoma.

The relevant literature lacks detailed numerical data about skin tags.¹¹ They are benign connective tissue tumors of the dermis, soft, skin-colored, pedunculated, or filiform. They occur frequently and usually do not cause discomfort. Banik and Lubach¹¹ reported on the frequency of skin tags according to sex, age, and location in 750 unselected patients (Table 1); 348 persons (46 percent) had skin tags, and the frequency increased up to the fifth decade but not beyond. In this study, 248 (71.3 percent) had 1–3 skin tags, 50 (14.4 percent) had 4–7 skin tags, and 50 (14.4 percent) had more than 7 skin tags. The authors concluded that almost every second person was a skin tag carrier.

Literature Review: Positive and Negative Correlations

In 1983, Leavitt, et al. reported on 94 men (mean age was 54.5 ± 1.2 years) at the Miami Veterans Administration Hospital who were referred for colonoscopy.⁸ The patients were examined for skin tags before undergoing the procedure, and

Table 1. Frequency of Skin Tags in Relation to Sex and Age (Study by Banik and Lubach¹¹).

Sample (n = 750)*	Skin Tags Present	Skin Tags Absent
Men = 387 (51%)	192 (25%)	195 (26%)
Women = 363 (49%)	156 (21%)	207 (28%)

* Age range = 1–99 years; mean = 50 years.

Table 2. Ratio of Skin Tags to Polyps (Study by Leavitt, et al.⁸).

	Polyps	
	Yes	No
Skin Tags		
Yes	37 (39%)	11 (12%)
No	9 (10%)	37 (39%)

the data showed that skin tags provided a sensitivity of 80.4 percent and a specificity of 77.1 percent, with a 19.6 percent false-negative rate and a 22.9 percent false-positive rate (Table 2).⁸

In 1985, Kune, et al. studied 100 consecutive patients scheduled for colonoscopy after pre-examination screening for skin tags.⁴ There were 76 men and 24 women (mean age was 67.2 years). The data showed skin tags provided a sensitivity of 80 percent and a specificity of 58 percent, with a 20 percent false-negative rate and a 42 percent false-positive rate (Table 3).⁴

That same year, Chobanian, et al. published a study of symptomatic patients consisting of 61 men and 39 women consecutively evaluated by colonoscopy (mean age was 53.55 years \pm 15.9 years) and found the association of skin tags with adenomatous polyps to have a sensitivity of 73 percent and specificity of 71 percent. This gave a 27 percent false-negative rate and 29 percent false-positive rate (Table 4).¹²

Chobanian, et al.¹³ again reported in 1986 a study of 96 persons (55 men and 41 women; mean age, 56.25 years) who were healthy volunteers without indication for colonic investigation. All were screened for skin tags and subsequently underwent air contrast barium enema and pan-colonoscopy. Thirty-four percent had polyps, and 53 percent of those with polyps also had skin tags.

Table 3. Relation of Skin Tags to Polyps and Colorectal Disease (Study by Kune, et al.⁴).

	Skin Tags		Total
	Yes	No	
Adenomatous polyps	36	9	45
Colorectal cancer	5	6	11
Other colorectal disease	15	15	30
Normal study	3	11	14
Total	59	41	100

Table 4. Ratio of Skin Tags to Polyps (Study by Chobanian¹²).

	Polyps	
	Yes	No
Skin Tags		
Yes	30	11
No	17	42

The overall calculated odds ratio showed those with skin tags had approximately a twofold greater risk for colonic polyps than the general population, and those in the subgroup aged < 50 years had a risk factor of 6.2.¹³

Also in 1986, Beitler, et al. reported on 54 patients (33 men and 21 women; mean age, 66 years) who were referred for colonoscopy. All were screened before colonoscopy for skin tags, and the results showed the sensitivity was 86 percent and the specificity was 58 percent.¹⁴

Eckardt¹⁵ suggested further investigation of healthy persons with skin tags to determine the importance of the association between skin tags and colon neoplasia. He reported on 750 patients who were evaluated on an outpatient basis for colon disease, none of whom had a history of colon neoplasia. All were examined for skin tags, and 257 persons (34.26 percent) had them. More than five skin tags were found in each of 30 persons. Patients with multiple skin tags had an even higher risk of colon carcinoma.

Gould and colleagues studied 492 patients in a primary care setting; 251 were for screening and 241 were for symptoms. All were examined for skin tags, and the authors concluded that skin tags were not a marker for colon polyps.¹⁶ Most studies have been conducted in referral clinics where highly selective, symptomatic populations had colonoscopy; however, Gould's study was conducted in a primary care setting, and the patients were subjected only to a 60-cm flexible sigmoidoscope.

Luk and the colon-neoplasia work group studied the presence of skin tags as markers for colonic polyps. They concluded that there was no correlation between skin tags and colon polyps in families with the polyposis syndrome.¹⁷

Piette, et al.¹⁸ recently published data on a prospective study of 100 asymptomatic patients where no association was found between skin

tags and colonic polyps. They reviewed the literature and conducted a meta-analysis, which showed significant association between skin tags and colonic polyps in 777 symptomatic patients but no association in 268 asymptomatic patients. They concluded that skin tags constitute a marker for colonic polyps only in symptomatic patients for whom colonoscopy is already indicated; hence, their detection was of no diagnostic value in asymptomatic patients. However, it should be noted that these 777 symptomatic patients were probably born with or developed skin tags earlier than or simultaneously with colon polyps. If they had all been screened for the presence of skin tags before developing symptoms, a significant relation between skin tags and colon polyps might have been shown. In their 100 asymptomatic patients, the sensitivity of skin tags for identifying a patient with colon polyps was good (71 percent), but the specificity (40 percent) and positive predictive value (16 percent) were poor.

Dalton and Coghill, in 1985, on the basis of 100 consecutive autopsy examinations, reported that 57 percent had skin tags and 22 percent had colon polyps. This was not different from the prevalence in the general population.¹⁹

Chobanian²⁰ shared a gastroenterologist's perspective in 1987 by referring to Leavitt's work⁸ and several other published reports. He concluded that time alone will determine whether there is an association between skin tags and colon polyps in asymptomatic persons and the extent of its impact on colorectal cancer screening. On the other hand, the hypothesis may shrink with careful scrutiny and large controlled studies.

Genetic Relations

Genetic relations among skin tags, colon polyps, and colon cancer need ongoing clinical and genetic research. Although the clinical observation is suggestive of an association, there is presently no scientific way to prove this contention. In order to prove a genetic relation, blood samples from grandparents, parents, and children would need to be examined with specific DNA probes.^{21,22} These genetic probes are still under development and are of limited clinical reliability. The genetic basis for carcinogenesis and the diagnosis of genetic disorders at the DNA level are fascinating

research topics that have provided an increased understanding of the biochemical mechanisms of several diseases and basic defects at the DNA level.

Metzmaker and Sheehan²³ and Welter, et al.²⁴ have suggested that until phenotypic, genotypic, cytogenetic, immunologic, biochemical, or virologic markers are detected, other methods of surveillance for colorectal cancer are important.

Other Methods

Another investigative method is the water-suppressed proton nuclear magnetic resonance spectroscopy of plasma. This has been reported to be a potentially valuable approach to the detection of cancer.²⁵

In the absence of any specific tumor markers for colorectal cancer, physicians at the primary care level need to rely extensively on family history and personal history for detecting high-risk groups.^{26,27} I believe that patients with large skin tags should be evaluated more closely. The studies by Leavitt,⁸ Kune,⁴ Chobanian,^{12,13,20} Beitler,¹⁴ and Eckardt¹⁵ all point to the possible relation between skin tags and colon tumors.

Winawer, et al.²⁸ have explained clearly the various diagnostic methods in both symptomatic and asymptomatic patients. General guidelines need to be followed in all patients; however, the identification of persons at higher than average risk is the responsibility mainly of the primary care physician.

Lead Time Bias

Bias is a liability at any stage of inquiry, and it tends to produce results that drift from true values. Specific biases that occur in screening are particularly important in studies of colon polyps and cancer.

Lead time is the period of time between the detection of the polyp by screening and its detection when it is symptomatic. The lead time is dependent on the rate of progression of the disease (polyp) and the ability of the screening test to detect the disease at an early stage. If the lead time is short, the treatment of the disease detected on screening might be no more effective than treatment after symptoms appear. When lead time is long, the treatment of the disease detected at screening might be very effective. On

the face of it, screening appears to help people live longer.^{29,30}

To avoid lead time bias, it is necessary to study both a screened group of persons and a comparable control group to compare age-specific mortality rates from the time of diagnosis.^{28,29}

Length time bias occurs because a greater number of slow-growing lesions (polyps) are detected during screening compared with regular routine medical care. Screening tends to find polyps that inherently have a better prognosis, whereas routine care finds lesions with a worse prognosis.²⁹

Selection Bias

This bias occurs when comparisons are made between groups of patients who differ in respect to determinants of outcome beyond the ones that are under study.²⁹

Screening

Studies have shown that cancers detected by screening were at a less advanced pathological stage. However, whether screening and detection of early lesions have any effect on mortality is yet unclear. Our knowledge about enhanced life span subsequent to polyp removal is incomplete.³⁰

It is noteworthy also that an interesting syndrome — neurofibromatosis — consists of two separate genetic disorders (NF-1 and NF-2), which manifest as tumors surrounding nerves. These tumors consist of proliferated Schwann cells and fibroblasts with large amounts of extracellular matrix and collagen. Cutaneous signs include *café au lait* macules. There is no relation between the spots, their location and number, and the severity of disease.³¹⁻³³ Cutaneous neurofibromas are small soft tumors. Crowe³⁴ has established diagnostic criteria for classic NF-1, which include a minimum of 5 *café au lait* spots, each measuring 1.5 cm in diameter.

Whether a similar relation exists between skin tags and colon polyps needs further clinical investigation.

Conclusion

In light of the evidence in the medical literature to date, skin tags need to be considered a significant risk factor for polyps of the colon.

There is suggestion in the literature of increased risk when skin tags occur in patients less than 50 years of age.^{6,9,13} This may be explained

by the fact that skin tags, like colon polyps, occur more frequently with increasing age; therefore, their presence in a younger patient may represent an even stronger tendency toward development of polyps.

On the other hand, whether identification and removal of colon polyps enhances life span is not a scientifically proved fact. The positive implications of early diagnosis and intervention call for physicians to remain alert for the presence of any risk factors and to offer timely advice for screening evaluation if we are to improve the present mortality and morbidity from colorectal cancer.

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