Colorectal Villous and Tubulovillous Adenomas Equal to or Greater than Four Centimeters

JAROSLAV P. STULC, M.D., NICHOLAS J. PETRELLI, M.D., LEMUEL HERRERA, M.D., AND ARNOLD MITTELMAN, M.D.

The records of 237 patients treated for benign and malignant villous and tubulovillous adenomas at Roswell Park Memorial Institute from 1963 to 1987 were reviewed. Sixty-five adenomas were ≥4 cm and form the basis of this report. Fifteen (23%) were in the cecum, 3 (5%) in the right colon, 1 (1%) in the splenic flexure, 10 (15%) in the sigmoid colon, and 36 (55%) in the rectum. The most common symptoms were rectal bleeding (70%), mucus diarrhea (44%), constipation (22%), and tenesmus (19%). Fifty-five (85%) of these large adenomas contained invasive adenocarcinoma and one in situ carcinoma. Two thirds of invasive carcinomas arose from predominantly villous adenomas and one third from tubulovillous adenomas. Half of all malignant adenomas demonstrated metastases to regional lymph nodes or distant metastases. Seven malignant adenomas (12%) were associated with synchronous adenocarcinomas of the colon, and 29% of malignant adenomas were associated with synchronous adenomatous polyps, principally tubular type. Four of nine benign, large adenomas were associated with synchronous adenomas but with no adenocarcinomas. No relationship was found between the size of the adenoma, location, or Dukes' stage. Though the incidence of in situ and invasive carcinomas is clearly related to the size of the adenoma, a linear relationship could not be demonstrated.

From the Roswell Park Memorial Institute, Department of Surgical Oncology, Buffalo, New York

ADENOMAS of the colon and rectum represent true neoplastic growths and are generally regarded as potentially premalignant lesions. Villous and tubulovillous adenomas together constitute from 19–53% of colorectal adenomas.[1-3] The villous component has been implicated as the determinant more likely to be associated with in situ and invasive adenocarcinoma.[2-9] The other determinant has been directly related to size, with a proportionate increase in invasive carcinoma in larger lesions.[2,3,9-11] However, adenomas with a villous component are recognized for their ability to attain large dimensions without incurring concomitant malignancy, and invasive carcinoma is not uncommonly found in villous or tubulovillous adenomas <2 cm in size.[2,3,7,9-11] Given the uncertainty of malignant involvement in an adenoma, particularly of the larger lesions, various clinical and histologic criteria have been reported concerning polypectomy *versus* surgical resection.[7,12-16] Earlier reviews have advocated a conservative approach toward management of villous adenomas, even in the presence of invasive carcinoma, based on the contention that these lesions demonstrated a benign course with little predilection for metastases.[10,11,17]

Studies to date on colorectal adenomas have not discriminantly looked at large adenomas with a villous component; conversely, since the inception of the colonoscopy era, the literature has focused primarily on adenomas that can be removed by virtue of colonoscopy alone, often with the exclusion of malignant lesions.

The purpose of this review is to examine the clinical nature of villous and tubulovillous adenomas ≥4 cm in diameter and to correlate this with location of the lesions, incidences of in situ and invasive adenocarcinoma, and Dukes' staging.

Materials and Methods

This retrospective study reviews the medical records of 237 patients with villous or tubulovillous adenomas of the colon and rectum treated at Roswell Park Memorial Institute from 1963 to 1987. Only those patients with histologically confirmed benign and malignant villous and tubulovillous adenomas were included. Pa-

Reprint requests and correspondence: Nicholas J. Petrelli, M.D., Roswell Park Memorial Institute, Department of Surgical Oncology, 666 Elm Street, Buffalo, NY 14263.

Submitted for publication: July 14, 1987.

TABLE 1. *Site* Versus *Dukes' Stage of Malignant Villous Adenomas*

Site	Unknown	Dukes' Stage							
		A	B_1	B_2	B_3	C_1	C_2	C_3	D
Cecum	0	0	2	2	0	4	1	0	4
Right colon	0	0	1	0	0	1	0	0	0
Sigmoid	0	1	3	2	0	1	0	0	1
Rectum	0	0	7	6	1	8	0	2	5
Total (N = 56)	4	1	13	10	1	14	1	2	10

tients with papillary adenocarcinoma, polypoid adenocarcinoma, and equivocal histologic diagnoses were excluded. By these criteria, six patients were excluded from the study, and of the remaining 231 patients, 63 patients (27%) had villous or tubulovillous adenomas ≥4 cm. Two patients each had two synchronous villous lesions greater than 4 cm in diameter, constituting a total of 65 villous tumors. There were 28 women and 35 men with a median age of 66 years (range: 45–82 years).

Dimensions of the villous tumors were measured along their greatest diameter. Direct measurements of the surgical specimen were available in all instances, and if this was at variance with measurements obtained on colonoscopy, the more conservative measurement was used. All tumors resected at Roswell Park Memorial Institute were subjected to lymph node clearance using alcohol extraction of fat and fixation of lymph nodes in cedar oil.[18] Pathologic staging was performed according to the Gastrointestinal Tumor Study Group (GITSG) as follows: Dukes' A: mucosal invasion; Dukes' B_1: tumor through mucosa but no serosal penetration; Dukes B_2: serosal penetration; Dukes' B_3: serosal penetration with direct involvement of adjacent organs; Dukes' C_1: 1–4 lymph nodes positive for tumor; Dukes' C_2: more than 4 positive lymph nodes; Dukes' C_3: involvement of adjacent organ and positive lymph nodes; and Dukes' D: distant metastases. Patients were analyzed according to the site of primary villous tumor, frequency of benign *versus* malignant adenoma, pathologic stage in regards to site of the primary lesion and size, and site of the tumor in relation to size.

Results

Of 65 total villous tumors, 55 (85%) were found to contain invasive adenocarcinoma, defined as invasion through the muscularis mucosa, and one tumor (1%) contained *in situ* adenocarcinoma. The remaining nine (14%) villous tumors contained no foci of carcinoma. Twenty-one villous tumors were diagnosed prior to 1973 by barium enema and proctosigmoidoscopy, of which only two adenomas were found to be benign. Forty-four additional villous tumors were diagnosed after 1973, principally by colonoscopy, and 37 of these contained adenocarcinoma. The location of the primary villous tumors was as follows: cecum, 15 (23%): 13 contained carcinoma and two were benign; ascending colon, three (5%): two contained carcinoma and one was benign; splenic flexure, one was benign; sigmoid, 10 (15%): eight contained carcinoma and two were benign; rectum, 36 (55%): 33 contained carcinoma and three were benign.

Though the number of villous tumors of the rectum diagnosed prior to and after the institution of colonoscopy were similar (16 and 20, respectively), three malignant villous adenomas of the right colon and one of the sigmoid were diagnosed prior to 1973, while 12 malignant villous adenomas of the right colon and seven of the sigmoid were diagnosed subsequent to the introduction of colonoscopy.

Fifty-six villous or tubulovillous adenomas contained carcinoma. In each case, clear demarcation or transition from benign villous or tubulovillous component to *in situ* or invasive carcinoma was apparent on histologic examination. Since all carcinomas arose either centrally or along one border of the adenoma, measurements were based on the extent of the grossly benign component. The adenocarcinomas were as follows: one Dukes' A, 13 Dukes' B_1, ten Dukes' B_2, one Dukes' B_3, 14 Dukes' C_1, one Dukes' C_2, 2 Dukes' C_3, and ten Dukes' D carcinomas (Table 1). In four additional rectal villous adenomas with invasive carcinoma, Dukes' staging was not possible because three patients refused abdominoperineal resection following transanal or transsacral resection of the villous adenoma, and one patient underwent transanal resection of a malignant villous adenoma in conjunction with right hemicolectomy for a synchronous cecal adenocarcinoma. Of 15 malignant villous adenomas of the cecum and right colon, 66% were metastatic to lymph nodes, and of 29 staged malignant villous adenomas of the rectum, 50% were metastatic to lymph nodes (Table 1).

Differentiation of the 55 villous adenomas with invasive carcinoma was as follows: well differentiated, 27; moderately well differentiated, 26; poorly differentiated,

2; and one *in situ* adenocarcinoma. The degree of differentiation of the tumor bore no relation to the site or size of the primary.

Clinically, the most frequent symptoms were rectal bleeding (44 patients) and a change in bowel habits (38 patients), with mucus diarrhea being twice as frequent as constipation. Eight patients experienced tenesmus, six patients experienced vague, crampy abdominal pain, six noted weight loss, one noted a decrease in stool caliber, and one had prolapse of a rectal tumor. Two patients presented with anemia and six patients were asymptomatic with a lesion found either on routine examination of the lower gastrointestinal tract or by fecal occult blood. No patients experienced the syndrome of voluminous diarrhea and hypokalemia. The range of duration of symptoms was from 1 month to 8 years, with a median of 7 months.

Fifty-nine patients underwent 64 procedures for excision or resection of their villous tumor (Table 2). Two patients with metastatic disease underwent colonoscopy only and biopsies of the tumor, and one large villous adenoma was found incidentally at autopsy. Seven patients (12%) had synchronous invasive adenocarcinomas of the colon that did not arise in association with an adenoma. A total of 40 synchronous adenomas of the colon and rectum were found in 16 of the 56 patients (29%) with malignant villous adenomas. The majority of these adenomas were tubular, and of these, one patient had six tubular adenomas of varying size concomitantly with two synchronous malignant, large villous adenomas. Two patients had tubulovillous adenomas containing invasive carcinomas. The remaining polyps were an even distribution of tubular, villous, and mixed tubulovillous adenomas, with the majority containing *in situ* carcinomas. Three of 9 (33%) benign, large villous adenomas were associated with a total of 22 synchronous benign adenomas. One patient harbored 16 tubular adenomas in association with a benign cecal villous adenoma.

In contrast to the adenomas synchronous with malignant, large villous adenomas, the adenomas synchronous with benign, large villous adenomas were in no instance found to contain either *in situ* or invasive adenocarcinomas. Furthermore, in both benign and malignant villous adenomas, the associated adenomas were principally located in the same segment of colon or rectum with the primary villous adenoma.

TABLE 2. *Surgical Procedures for Villous and Tubulovillous Adenomas**

Procedure	Number of Villous Adenomas Without Carcinoma	Number of Villous Adenomas With Carcinoma	Total
Exploratory laparotomy	0	1	1
Total proctocolectomy	0	2	2
Right colectomy	3	11	14
Left colectomy	1	1	2
Sigmoidectomy	0	5	5
Low anterior resection	1	2	3
Abdominoperineal resection	1	17	18
Kraske procedure	1	2	3
Transanal resection	1	6	7
Fulguration†	0	2	2
Polypectomy	1	3	4

* Two patients with metastatic carcinoma (rectal and cecal adenoma) underwent colonoscopy and biopsies of the primary lesion only; one patient had the adenoma found incidentally at the time of autopsy.

† One patient subsequently underwent abdominoperineal resection, and the other patient underwent subsequent low anterior resection.

In regards to metachronous adenocarcinoma of the colon, two patients with malignant villous adenomas of the rectum subsequently developed adenocarcinomas of the right colon within several years, and one patient with a malignant cecal villous adenoma developed adenocarcinoma of the transverse colon 18 months following resection of the first primary. Three patients with malignant villous adenomas of the cecum had previously undergone resection of sigmoid adenocarcinomas. Follow-up concerning metachronous adenomas, however, has not been sufficient to allow for significant data.

The size of the villous and tubulovillous adenomas ranged from 4–20 cm. Four malignant villous adenomas (two cecal and two rectal) were annular but exceeded 4 cm in diameter longitudinally. For benign and malignant villous and tubulovillous adenomas, the mean diameters were 5 cm. The site of the adenoma had no correlation with its size (Tables 3 and 4). When the

TABLE 3. *Size (cm) of Villous Adenomas Without Carcinoma Related to Bowel Site*

Site	Mean	4–4.9	5–5.9	6–6.9	7–7.9	8–8.9	9–9.9	10–10.9	>11
Cecum	4.0	1	0	0	0	1	0	0	0
Right colon	6.0	0	0	1	0	0	0	0	0
Splenic flexure		0	0	1	0	0	0	0	0
Sigmoid	5.5	1	0	0	1	0	0	0	0
Rectum	6.0	2	0	0	0	1	0	0	0

TABLE 4. *Size (cm) of Villous Adenomas With Carcinoma Related to Bowel Site*

Site	Mean	4–4.9	5–5.9	6–6.9	7–7.9	8–8.9	9–9.9	10–10.9	>11
Cecum	7.6	1	2	2	0	1	2	1	1
Right colon	5.0	1	0	1	0	0	0	0	0
Sigmoid	5.5	4	3	0	0	1	0	0	0
Rectum	5.5	12	10	2	3	3	0	1	1

Dukes' stage of malignant villous adenomas was compared to the mean size, no correlation was found (Table 5). In four malignant adenomas of indeterminable Dukes' stage, mean diameter was 5.5 cm, and one villous adenoma with *in situ* carcinoma was 5 cm in diameter. Thirteen Dukes' B_1 tumors had a mean diameter of 7.6 cm, but this included two large villous adenomas of 14 and 20 cm, respectively. Ten Dukes' B_2 carcinomas had a mean diameter of 5.8 cm; one Dukes' B_3 tumor was 10 cm, one Dukes' C_2 carcinoma was 5 cm, two Dukes' C_3 tumors were 6 cm, and ten Dukes' stage D adenocarcinomas were 5.4 cm in mean diameter. Therefore, the size that a villous adenoma can attain does not appear to be significantly modified by its location in the colon or rectum. Similarly, the presence or absence of malignancy and the pathologic stage of a malignant villous adenoma clearly are not related to location of the primary adenoma nor to its size (Tables 3–5).

Discussion

Adenomas of the colon and rectum are generally regarded as premalignant lesions. Morphologically, adenomas are differentiated as either tubular, villous (papillary), or tubulovillous (villoglandular or mixed). The villous component was initially recognized as a distinct clinical entity with a significant potential for malignant transformation; the incidence of malignancy was directly proportional to size and degree of villous component.[19,20] Following the introduction of colonoscopy in 1973, the relationship between colorectal adenomas to the development of malignancy was conceptually developed.[1-11]

Though fiberoptic endoscopy is the preferred approach to the management of colonic polyps, particularly those that are pedunculated, the majority of villous and a significant number of tubulovillous adenomas are sessile. The endoscopic removal of larger sessile polyps entails increased morbidity and the increasing probability of incomplete resection with possible residual disease left behind. On the other hand, risk may outweigh benefit if the patient is subjected to a formal surgical procedure under circumstances in which there is a reasonable chance for benign disease.

Several large series have attempted to delineate criteria for further surgical intervention in adenomas with invasive carcinoma. The retrospective series by Wolff and Shinya[2] analyzed 892 endoscopically resected polyps, of which 57.3% were tubular adenomas, 29.2% were tubulovillous adenomas, and 12.4% were villous adenomas. Conversely, invasive cancer was most prevalent in villous adenomas (12.6%) followed by tubulovillous adenomas (3.8%) and tubular adenomas (3.3%). Invasive carcinomas were most frequent in larger and sessile lesions. This is a sanction confirmed by a later study by Shinya and Wolff[3] demonstrating that all gradations of cellular change from dysplasia to invasive carcinoma increased in all colon segments as the villous component of the adenoma increased. In the same series, when the villous adenoma was ≥3 cm in diameter, the incidence of carcinoma *in situ* was 33% *versus* 21.4% in tubulovillous adenomas. The incidence of in-

TABLE 5. *Size (cm) of Villous Adenoma With Carcinoma Related to Dukes' Stage*

Dukes' Stage	Mean	4–4.9	5–5.9	6–6.9	7–7.9	8–8.9	9–9.9	10–11	>11
Unknown	5.5	1	2	0	1	0	0	0	0
Dukes' A	5.0	0	1	0	0	0	0	0	0
Dukes' B_1	8.0	3	4	2	0	1	0	0	2
Dukes' B_2	5.8	4	1	0	1	1	1	0	0
Dukes' B_3	10.0	0	0	0	0	0	0	1	0
Dukes' C_1	5.0	5	4	3	0	1	1	0	0
Dukes' C_2	5.0	0	1	0	0	0	0	0	0
Dukes' C_3	6.0	0	1	0	1	0	0	0	0
Dukes' D	5.4	5	1	0	0	2	0	1	0
Total	6.1	18	15	5	3	5	2	2	2

vasive carcinoma was 13% *versus* 15%, respectively. Though polyp size was an important determinant for the presence of malignancy, invasive cancer was also found in polyps <1 cm in diameter. Furthermore, it has been recognized that adenomas with a predominantly villous component can attain large dimensions without developing invasive carcinoma.

Due to the fact that no previous studies had discriminately analyzed large colorectal adenomas with a predominantly villous morphology (greater than 60% of morphology), our study was undertaken. Based on the literature citing a significant increase in the frequency of carcinoma in villous adenomas >3–4 cm in diameter, an arbitrary lower limit of 4 cm was chosen. Of the 237 histologically documented villous and tubulovillous adenomas of the colon and rectum in a 24-year period extending from 1963 to 1987 at Roswell Park Memorial Institute, 65 cases of villous adenomas ≥4 cm were found. The incidence of invasive adenocarcinoma was found to be 85%. This is a significantly higher percentage than has been cited in the literature.[2,3,7,9,12] In comparison, Shinya and Wolff found the incidence of invasive carcinoma in villous and tubulovillous adenomas ≥3 cm to be on the order of 13–15%,[3] and Christiansen et al.[12] found a 48.5% incidence of invasive carcinoma in clinically benign villous colorectal adenomas >2 cm in diameter.[12] Muto et al.[7] reported a 46% incidence of invasive carcinoma in tubular and villous adenomas >2 cm. An incidence of invasive carcinoma of 32% was found in villous and tubulovillous adenomas >4 cm in diameter in a series of 1049 patients by Galandiuk et al.[9] In part, the high incidence of invasive carcinoma in our series may reflect the tertiary referral pattern of our institution. Another explanation may relate to the fact that a pathologist, when confronted with a colorectal surgical specimen obviously containing adenocarcinoma, directs attention to the confirmation of adenocarcinoma and may overlook or disclaim contiguous areas of benign adenoma. This may be particularly true in those larger lesions where the adenocarcinoma has overgrown the adenoma from which it initially arose. In small adenomas at an earlier stage of invasive carcinoma the predominant nature of the benign component and the transition into invasive carcinoma is more apparent.

The location of large villous and tubulovillous adenomas in our series was primarily in the right colon (28%) and the rectosigmoid (55%). A similar distribution of adenomas with a villous component has been reported in the literature,[2–16] though the frequency of cecal lesions was somewhat higher in our series. Approximately 50% of the malignant adenomas were located in the rectum, which is consistent with other studies.[9,10,12] The overall number of rectal adenomas diagnosed endoscopically remained the same before and after 1973, but four times as many cecal and right colon adenomas were noted following the introduction of colonoscopy. This may reflect a more accurate incidence of large villous and tubulovillous adenomas of the cecum and right colon, since these lesions classically are asymptomatic until they attain large size, can be readily missed by barium enema examination, and can be overlooked even by direct palpation or endoscopic examination.

In our series, 37 of 56 malignant adenomas were predominantly villous, 13 tubulovillous adenomas contained invasive adenocarcinoma, and three adenomas of each type contained both *in situ* and invasive carcinomas. In contrast, of the nine benign adenomas, four were predominantly villous and five were tubulovillous. The differentiation of the adenocarcinomas was evenly divided between well differentiated and moderately well differentiated, with only two poorly differentiated adenocarcinomas. Seventeen malignant villous and tubulovillous adenomas were noted to secrete large amounts of mucin. Five of these malignant adenomas were located in the right colon, one in the sigmoid, and 11 in the rectum. The Dukes' stage of mucin-secreting adenocarcinomas was uniformly distributed.

Seven of the 56 malignant adenomas (12%) had synchronous adenocarcinomas of the colon at the time of diagnosis. The incidence of malignancy is also directly proportional to the frequency of synchronous and metachronous adenomas.[3,9] In our series, 16 of 56 malignant adenomas (29%) were associated with 40 synchronous adenomas; the majority of these were tubular, with two containing invasive adenocarcinoma and seven containing carcinoma *in situ*. Interestingly, in virtually every instance, synchronous adenomas were found to be in the same segment of colon or rectum as the malignant primary adenoma.

Difficulty in assessing the presence of malignancy in larger polyps and the controversy regarding management of early invasive carcinomas in adenomas has led to the evolution of guidelines for management. Currently, the rationale for surgical intervention is predicated upon polyp size, sessile *versus* pedunculated, adequacy of margin, patient age, and the presence or absence of multiple synchronous or metachronous adenomas.[2,3] Further determinants also include the increased risk for carcinoma from 5–15 years for single adenomas and the male population older than 60 years of age.[15] Induration within a rectal villous adenoma has been suggested as a reliable clinical sign for the presence of invasive carcinoma.[13] Villous and tubulovillous adenomas in all segments of the colon and rectum and

through all ranges in size have a known propensity to develop carcinoma. The morphology of these polyps is predominately sessile. In spite of this, several reports have advocated a conservative approach toward the management of large villous adenomas on the premise that they can be benign and that even if invasive carcinoma is present it is rarely metastatic and follows a relatively benign course.[10,11,17,21] This is contradicted by literature that demonstrates a 28–46% incidence of invasive carcinoma in villous adenomas >3 cm and a metastatic potential.[3,7,8,9,16] Furthermore, the biopsy failure rates for identifying invasive adenocarcinoma in a villous adenoma are 40–50%.[10,12]

The local recurrence rate for surgical excision alone of a villous adenoma of the colon and rectum is 17–30%,[10,12] all recurrences presenting within the first five years. The recurrence rate for villous adenomas that have been fulgurated is significantly higher and the time interval to recurrence significantly shorter. The local recurrence of a benign villous adenoma has been associated with a 7.7% incidence of subsequent malignancy.[11] However, there is a trend among endoscopists to treat villous lesions of the colon and rectum that cannot be totally removed endoscopically with electrocoagulation or laser coagulation, thus not only increasing the likelihood of local recurrence but increasing the chances of failing to recognize invasive carcinoma.

In our series of 52 malignant villous adenomas in which the Dukes' stage was determined, over 50% of the malignant villous adenomas had metastasized to regional lymph nodes or were associated with distant metastases. Half of all metastases were to visceral organs without associated lymph node involvement, raising the possibility that invasive carcinomas arising within villous adenomas do not metastasize primarily via lymphatics. For invasive carcinomas arising in rectal adenomas, seven of 32 carcinomas recurred locally within the rectovaginal septum or within the true pelvis, and another three had extension to bladder, prostate, or pelvic wall at the time of initial exploration and resection.

We speculated that although tubular and villous adenomas represent variations in an otherwise general abnormal cellular change, villous adenomas carry a higher potential for malignancy that may be biologically predetermined at an early stage in the induction and growth of the polyp. Noting that *in situ* and invasive adenocarcinomas occur in villous adenomas irrespective of size, and that some villous adenomas attain very large sizes without incurring malignancy, it is conceivable that foci of *in situ* carcinoma arise early in these polyps and are recognizable and predetermined by the time the polyp reaches a size from of 1–2 cm. This is further supported by observations that invasive carcinomas within an adenoma were confined in our series to one focus and that the coexistence of several areas of invasive carcinoma within the same large villous or tubulovillous adenoma was never observed, even after careful histologic examination of serial sections. Furthermore, the coexistence of separate foci of *in situ* carcinoma in adenomas with invasive carcinoma was infrequent. There is, of course, the possibility that separate foci of invasive carcinoma rapidly coalesce and overtake the more indolent growth of the accompanying benign component. Further studies involving careful sectioning of all adenomas with *in situ* and invasive carcinoma to determine the incidence of concomitant malignant foci would be required.

Nevertheless, it is unlikely that villous and tubulovillous adenomas simply undergo malignant transformation beyond a certain critical dimension. The contention that all adenocarcinomas of the colon and rectum arise from preexisting adenomas is also arguable. More likely is the possibility that many colorectal adenocarcinomas either are contiguous with benign components that are not appreciated by the pathologist at the time of examination of the surgical specimen, or eventually destroy any continguous benign component. Lastly, the assumption that villous adenomas in general follow a benign course and that invasive adenocarcinomas arising within these adenomas are of low grade without significant metastatic potential is not supported by our study.

Summary

In our review of 65 villous and tubulovillous adenomas ≥4 cm in diameter, 85% demonstrated a focus of invasive adenocarcinoma. The principal locations of all adenomas were in the right colon and rectosigmid region. The most frequent site of malignant tumors was in the rectum (58%), the right colon (27%), and sigmoid colon (15%). There was no relationship between size of the adenoma, location of the adenoma, or Dukes' stage. Half of all malignant adenomas demonstrated metastases to regional lymph nodes or distant metastases. Though the incidence of invasive and *in situ* carcinomas is clearly related to size of the adenoma, a linear relationship between size and incidence of malignancy could not be demonstrated in adenomas ≥4 cm. It is therefore postulated that adenomas with a predominant villous component to their morphology are biologically predetermined at an early stage in the growth of the neoplasm to manifest cellular changes capable of leading to malignancy. Otherwise, the neoplasm retains the capacity to attain large dimensions without ever incurring malignancy.

References

1. Konishi F, Morson BC. Pathology or colorectal adenomas: a colonoscopic survey. J Clin Pathol 1982; 35:830–841.
2. Wolff WI, Shinya H. Definitive treatment of "malignant" polyps of the colon. Ann Surg 1975; 182:516–525.
3. Shinya H, Wolff WI. Morphology, anatomic distribution and cancer potential of colonic polyps. Ann Surg 1979; 190:679–683.
4. Enterline HT, Evans GW, Mercado-Lugo R, et al. Malignant potential of adenomas of colon and rectum. JAMA 1962; 179:322–330.
5. Grinnell RS, Lane N. Benign and malignant adenomatous polyps and papillary adenomas of the colon and rectum. Surgery 1958; 106:519–538.
6. Kaneko M. Pedunculated adenomatous polyps of the colon and rectum with particular reference to their malignant potential. Mt Sinai J Med (NY) 1972; 39:103–111.
7. Muto T, Bussey HJR, Morson BC. The evolution of cancer of the colon and rectum. Cancer 1975; 36:2251–2270.
8. Coutsoftides T, Sivak MV, Benjamin SP, et al. Colonoscopy and the management of polyps containing invasive carcinoma. Ann Surg 1978; 188:638–641.
9. Galandiuk S, Fazio VW, Jagelman DG, et al. Villous and tubulovillous adenomas of the colon and rectum: a retrospective review, 1964–1985. Am J Surg 1987; 153:41–47.
10. Jahadi MR, Baldwin A Jr. Villous adenomas of the colon and rectum. Am J Surg 1975; 130:729–732.
11. McCabe JC, McSherry CK, Sussman EB, et al. Villous tumors of the large bowel. Am J Surg 1973; 126:336–342.
12. Christiansen J, Kirkegaard P, Ibsen J. Prognosis after treatment of villous adenomas of the colon and rectum. Ann Surg 1979; 189:404–408.
13. Pheils MT. Villous tumors of the rectum. Dis Colon Rectum 1979; 22:406–407.
14. Nivatvongs S, Nicholson JD, Rothenberger DA, et al. Villous adenomas of the rectum: the accuracy of clinical assessment. Surgery 1980; 87:549–551.
15. Morson BC, Bussey HJR. Magnitude of risk for cancer in patients with colorectal adenomas. Br J Surg 1985; 72:23–25.
16. Wilcox GM, Anderson PB, Colacchio TA. Early invasive carcinoma in colonic polyps: a review of the literature with emphasis on the assessment of the risk of metastasis. Cancer 1986; 57:160–171.
17. Parks AG, Stuart AE. The management of villous tumors of the large bowel. Br J Surg 1973; 60:688–695.
18. Pickren JW. Nodal clearance and detection. JAMA 1975; 231:969–971.
19. Sunderland DA, Binkley GE. Papillary adenomas of the large intestine: a clinical and morphological study of forty-eight cases. Cancer 1948; 1:184.
20. Wheat MW, Ackerman LV. Villous adenomas of the large intestine: clinicopathologic evaluation of 50 cases of villous adenoma with emphasis on treatment. Ann Surg 1958; 147:476–486.
21. Thomson JPS. Treatment of sessile villous and tubulovillous adenomas of the rectum: experience of St. Mark's Hospital, 1963–1972. Dis Colon Rectum 1977; 20:467–472.