

# Is Colonoscopy Needed for the Nonadvanced Adenoma Found on Sigmoidoscopy?

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See editorial on page 777.

**Background & Aims:** The need for colonoscopy when small tubular adenomas with low-grade dysplasia are found on sigmoidoscopy is uncertain. The aim of this study was to examine the prevalence and characteristics of proximal adenomas in patients with distal adenomas. **Methods:** We studied 981 subjects with distal adenomas found on the index colonoscopy before randomization in the Polyp Prevention Trial. **Results:** Four hundred sixty patients (46.9%) had  $\geq 1$  distal adenoma that was pathologically advanced (villous component, high-grade dysplasia, or  $\geq 1$  cm); 21.5% (211 of 981) had any proximal adenoma; and 4.3% (42 of 981) (95% confidence interval [CI], 3.0–5.5) had an advanced proximal adenoma. A greater percentage of patients with an advanced distal adenoma (5.9%) (95% CI, 3.7–8.0) had an advanced proximal adenoma compared with those with a nonadvanced distal adenoma (2.9%) (95% CI, 1.4–4.3) (OR, 2.1; 95% CI, 1.1–4.3;  $P = 0.03$ ). Not performing a colonoscopy in patients with a nonadvanced distal adenoma would have missed 36% (15 of 42) of the advanced proximal adenomas. **Conclusions:** Patients with an advanced distal adenoma are twice as likely to have an advanced proximal adenoma as patients with a nonadvanced distal adenoma. However, eschewing a colonoscopy in patients with a nonadvanced distal adenoma would result in not detecting a sizeable percentage of the prevalent advanced proximal adenomas. These data support performance of a colonoscopy in patients with a nonadvanced distal adenoma. Confirmation of these results in asymptomatic subjects undergoing screening sigmoidoscopy is advisable.

The need for colonoscopy in individuals with small tubular adenomas with low-grade dysplasia found on sigmoidoscopy is an important and controversial issue in screening for colorectal cancer. The current standard recommendation that colonoscopy is needed when adenomas are discovered on flexible sigmoidoscopy<sup>1-5</sup> is based on an approximate 30% prevalence of a synchronous proximal adenoma.<sup>6-24</sup> However, colonoscopy for the 10%–13%<sup>25</sup> of individuals with a histologically confirmed adenoma on sigmoidoscopy adds considerably to the cost of screening,<sup>26</sup> especially when the costs of subsequent surveillance are included.

Studies of the natural history of adenomatous polyps are limited but show that individuals with advanced polyps, such as those with tubulovillous or villous histology,<sup>27</sup> large polyps ( $\geq 1$  cm),<sup>27-30</sup> or polyps with high-grade dysplasia,<sup>27</sup> are at increased risk for mortality from colorectal cancer. In contrast, individuals with single or multiple small ( $\leq 1$  cm) nonadvanced tubular adenomas removed during rigid sigmoidoscopy<sup>27</sup> or with small polyps that were fulgurated<sup>31</sup> were not at increased risk for mortality to colorectal cancer.

In an attempt to limit costs, large health maintenance organizations including the massive Kaiser–Oakland screening sigmoidoscopy program<sup>32</sup> and some clinical trials<sup>33,34</sup> are not routinely pursuing colonoscopy in individuals with tubular adenomas  $< 1$  cm in size found on flexible sigmoidoscopy.

*Abbreviations used in this paper:* CI, confidence interval; OR, odds ratio; PPT, Polyp Prevention Trial.

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Several small studies suggest that the prevalence of advanced adenomas in the proximal colon in individuals with nonadvanced distal adenomas is infrequent. In the study of 206 patients by Zarchy and Ershoff, individuals with advanced distal adenomas found on sigmoidoscopy were 16 times more likely than individuals without an advanced distal adenoma to have an advanced proximal adenoma, and the prevalence of an advanced proximal adenoma in the absence of an advanced distal adenoma was only 0.8%.<sup>20</sup> Other studies have reported a prevalence of advanced adenomas in the absence of advanced distal adenomas as low as zero.<sup>22</sup> In a recent prospective study of 203 patients with a distal adenoma on sigmoidoscopy, Read et al. found an overall prevalence of advanced proximal adenomas of 8.4% (17 of 203), with a 6% prevalence of an advanced proximal adenoma among patients with a distal adenoma  $\leq 5$  mm.<sup>21</sup> They concluded that colonoscopy was indicated for all patients with distal adenomas, regardless of the characteristics of the distal adenoma. In that sample, however, there were three cancers, seven times what would be expected from SEER (Surveillance, Epidemiology, and End Results) data,<sup>35</sup> which raises concern about the generalizability of conclusions from that population.

The prevalence of advanced proximal adenomas is low (only 3% in autopsy studies<sup>13,36-40</sup> and  $<10\%$  in clinical studies) whether subjects were surveyed for screening, follow-up of clinical symptoms, or because of family or personal history of polyps or cancer.<sup>13,20-22,41</sup> Because of the low prevalence, large studies are needed to have sufficient power to be confident of the estimate and the purported relationships between distal and proximal adenoma characteristics.

The Polyp Prevention Trial (PPT) is a large ( $N = 2079$ ) ongoing, multicenter randomized study of dietary intervention on adenoma recurrence. The details of the rationale, design, recruitment, and baseline characteristics of the study population have been reported.<sup>42,43</sup> The PPT cohort is useful for study of the relationship between distal and proximal adenomas because of its large size, diverse geographic representation, careful documentation of patient and polyp characteristics, the requirement for complete examination of the colon, and the independent pathological review to which all specimens are subjected.

## Patients and Methods

### Study Population

A detailed description of the determination of eligibility and randomization of participants in the PPT has been reported.<sup>42</sup> Participants were recruited from academic and community hospitals in the vicinity of eight regional clinical

centers: Bowman Gray School of Medicine, State University of New York at Buffalo, Edward Hines, Jr. Veterans Affairs Hospital, Kaiser Foundation Research Institute, Memorial Sloan-Kettering Cancer Center, University of Pittsburgh, University of Utah, and the Walter Reed Army Medical Center. A total of 2079 or 5.4% of 38,277 individuals undergoing colonoscopy and polypectomy who were screened for participation were successfully enrolled in the trial. The eligibility criteria included (1) age  $>35$ ; (2) one or more histologically confirmed adenomas removed within the previous 6 months; (3) complete removal of all polyps at baseline colonoscopy; and (4) complete colonoscopy to the cecum with adequate bowel preparation to identify and remove all polyps. Individuals were enrolled on the basis of having an adenomatous polyp and were not selected by the characteristics, number, or distribution of their adenomas. Participants could not have had a history of prior colorectal cancer, a previous large bowel resection, a history of a polyposis syndrome or inflammatory bowel disease, invasive carcinoma in any of the removed polyps, a body weight  $>150\%$  of the recommended level, or any unusual dietary habits that would have compromised the planned dietary intervention.

### Data Collection and Definitions

Data forms were collected by the clinical centers and submitted to a central office for data management (Westat, Rockville, MD). The index colonoscopy was defined as the colonoscopy that determined entry into the trial. By definition, all PPT subjects had one or more adenomatous polyps. The endoscopists' colonoscopy report was the source of information on size, multiplicity, and anatomic location of polyps. Adenomas were defined as advanced if the polyp had a villous component, high-grade dysplasia, or size  $\geq 1$  cm. All polyps were reviewed by two pathologists (K.J.L. and H.D.A.) for histological classification and assessment of the degree of atypia (low- vs. high-grade dysplasia). Adenomas designated as having a villous component were either villous or tubulovillous, with  $>75\%$  or 25%–75% villous architecture, respectively, in conformance with the conventions used for the National Polyp Study.<sup>44</sup> Adenomas were defined as distal if they came from the descending colon or more distally (in the sigmoid colon or rectum) or, when site was not available, located at  $\leq 50$  cm from the rectum by endoscopic measurement. Otherwise, the polyp was designated as proximal in location.

### Analysis

Comparisons of baseline continuous and binary data were performed with Student's *t* test and  $\chi^2$  test, respectively. Mantel-Haenszel adjusted odds ratios (ORs) were used to compare advanced adenoma characteristics between individuals with and without advanced distal adenomas. Exact *P* values and confidence intervals (CIs) were computed using the Stat-Xact3 program from Cytel Corp. (Cambridge, MA).

## Results

The derivation of the 981 patients used in this analysis is presented in Figure 1. Of the 2079 individuals enrolled in the PPT, 618 had previous adenomatous polyps and were excluded. Of the remaining 1461, 1123 had a confirmed distal adenoma. Additional 142 (12.6%) were excluded because of missing information. The missing data consisted of 137 patients with an adenoma of unknown size and 5 patients with an adenoma of unknown location (Figure 1).

In Table 1, the demographic data and polyp characteristics for the cohort are provided. The mean age was 60 years, 37.3% were female, 10.6% belonged to a minority, and >91% had a high school education. The indications for colonoscopy included 15.3% for positive fecal occult blood test, 22.4% for hematochezia, 53.0% for an abnormal barium enema or sigmoidoscopy, 7.4% for pain, and 25.5% for other reasons including family history, change in bowel habits, anemia, and others.

There were a total of 1576 adenomas in the 981 patients, 1251 of which were distal and 325 proximal. Of these adenomas, 17.9% had villous changes, 7.4% had high-grade dysplasia, and 27.7% were  $\geq 1$  cm. Of adenomas  $< 6$  mm, 6.4% had villous changes (53/830), and 2.9% had high-grade dysplasia (24/830). Of adenomas from 6 to  $< 10$  mm, 15.5% had villous changes

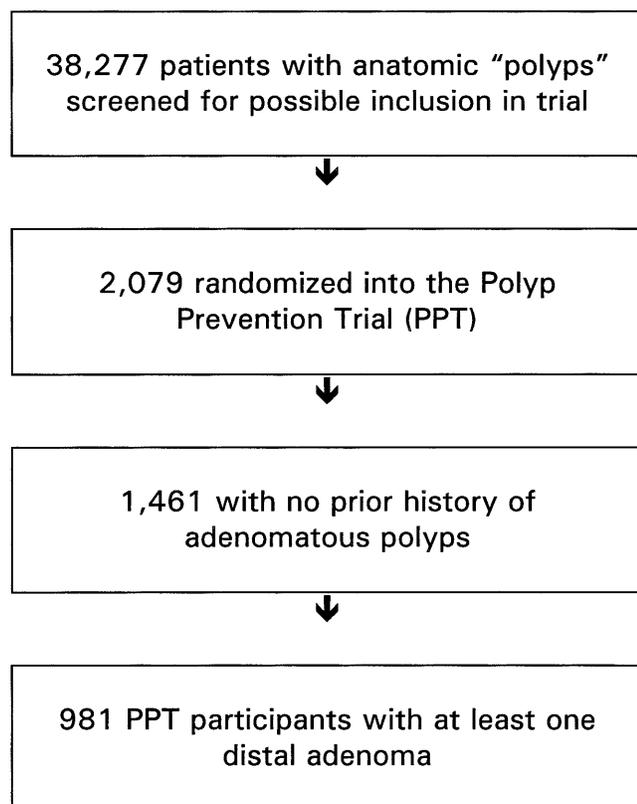


Figure 1. Derivation of the sample.

Table 1. Sample Characteristics

No. of patients	981
Age (yr)	60.0 $\pm$ 10.2 (SD)
Sex (% female)	37.3
Minority (%)	10.6
High school education (%)	91.6
Reasons for colonoscopy (%) <sup>a</sup>	
Positive FOBT	15.3
Hematochezia	22.4
After polyp found on BE or sigmoidoscopy	53.0
Pain	7.4
Other	25.5
% of patients (N = 981) with any distal adenoma with	
Villous histology	25.2
High-grade dysplasia	10.0
Size $\geq 1$ cm	37.5
Villous, high-grade dysplasia, or $\geq 1$ cm	46.9
% of patients (N = 211) with any proximal adenoma with	
Villous histology	8.1
High-grade dysplasia	4.7
Size $\geq 1$ cm	15.6
Villous, high-grade dysplasia, or $\geq 1$ cm	19.9

FOBT, fecal occult blood test; BE, barium enema.

<sup>a</sup>May have more than one reason for colonoscopy.

(48/310) and 4.5% had high-grade dysplasia (14/310), and of adenomas  $\geq 1$  cm, 41.5% had villous changes (181/436) and 17.9% had high-grade dysplasia (78/436). Distal adenomas measuring  $< 6$  mm were more likely to have villous changes than proximal adenomas of a similar size (8.4% [50/598] vs. 1.3% [3/232];  $P < 0.001$ ), but the incidence of high-grade dysplasia was similar (3.3% for distal adenomas vs. 1.7% for proximal;  $P = \text{NS}$ ).

Four hundred sixty patients (46.9%) had at least one distal adenoma with either villous changes, high-grade dysplasia, or which measured  $\geq 1$  cm (Table 1). Two hundred eleven patients (21.5%) had a proximal adenoma in addition to their distal adenoma. Of the patients with proximal adenomas, 19.9% (42/211) had a proximal adenoma with advanced pathological features (Table 1). The overall prevalence of advanced proximal adenomas in this cohort of 981 patients with distal adenomas was 4.3% (95% CI, 3.0–5.5) (42/981) (Table 2).

The relationships between distal adenomas and proximal adenomas with advanced pathological features for each of the three components of an advanced adenoma, villous histology, high-grade dysplasia, and size  $\geq 1$  cm, and for the combination of all three are presented in Table 3. Of patients with a distal adenoma with a villous

Table 2. Prevalence of Advanced Proximal Adenomas

Villous histology	1.7%
High-grade dysplasia	1.0%
Size $\geq 1$ cm	3.4%
Villous high-grade dysplasia or $\geq 1$ cm	4.3%

**Table 3.** Relationship Between Distal Adenomas and Advanced Proximal Adenomas

	% With proximal advanced <sup>a</sup>	OR (95% CI)	P value
Villous histology			
Distal villous	5.7 (14/247)	1.5 (0.7–3.0)	NS
Distal nonvillous	3.8 (28/734)		
HGD			
Distal HGD	7.1 (7/98)	1.9 (0.7–4.4)	NS
Distal, no HGD	4.0 (35/883)		
Size ≥1 cm			
Distal ≥1 cm	5.7 (21/368)	1.7 (0.9–3.3)	NS
Distal <1 cm	3.4 (21/613)		
Combined			
Distal villous, or HGD, or ≥1 cm	5.9 (27/460)	2.1 (1.1–4.3)	0.03
Distal nonvillous, no HGD, and <1 cm	2.9 (15/521)		

HGD, high-grade dysplasia.

<sup>a</sup>Villous histology, HGD, or size ≥1 cm.

component, 5.7% had a proximal advanced lesion compared with 3.8% of patients with a distal adenoma without a villous component (OR, 1.5; 95% CI, 0.7–3.0;  $P = \text{NS}$ ). Of patients with a distal adenoma with high-grade dysplasia, 7.1% had an advanced proximal lesion compared with 4.0% of patients with a distal adenoma without high-grade dysplasia (OR, 1.9; 95% CI, 0.7–4.4;  $P = \text{NS}$ ). Of patients with a distal adenoma ≥1 cm, 5.7% had a proximal advanced lesion compared with 3.4% of patients without a distal adenoma ≥1 cm (OR, 1.7; 95% CI, 0.9–3.3;  $P = \text{NS}$ ). Overall, 5.9% of patients (95% CI, 3.7–8.0) (27/460) with a distal advanced lesion compared with 2.9% of patients (95%

CI, 1.4–4.3) (15/521) without a distal advanced lesion had a proximal advanced lesion (OR, 2.1; 95% CI, 1.1–4.3;  $P = 0.03$ ). Not performing a colonoscopy in patients with a distal nonadvanced adenoma in this cohort would have missed 36% (15/42) of the proximal advanced adenomas.

A detailed accounting of the characteristics of the distal and proximal polyps in the 15 patients with nonadvanced adenomas distally but advanced adenomas proximally is provided in Table 4. Ten of these 15 had only a single distal adenoma measuring <6 mm. Of the 316 patients with a single distal nonadvanced adenoma measuring <6 mm, 70 (22.2%) had a proximal adenoma and 10 of 316 (3.2%) had an advanced proximal adenoma. Of 85 patients with multiple distal nonadvanced adenomas measuring <10 mm, 27 (31.8%) had a proximal adenoma and 2 (2.4%) had an advanced proximal adenoma.

Because this analysis was based on colonoscopy results, the definition of a distal as opposed to a proximal lesion was manipulated, and the analysis was repeated. Expanding the definition of a distal adenoma to include polyps in the splenic flexure or up to 60 cm or contracting the definition to include polyps in the sigmoid colon or up to 40 cm did not change the results (Table 5). Regardless of the definition, a similar percent of advanced proximal adenomas would have been missed had a colonoscopy not been performed for a distal nonadvanced adenoma (Table 5).

A stratified analysis by age and gender showed that the direction and magnitude of the relationship between a

**Table 4.** Detailed Characteristics of Participants With Nonadvanced Distal Adenomas but Advanced Proximal Adenomas

Patient	Age (yr)	Sex	Family <sup>a</sup> history	Distal count	Distal size (cm)	Proximal count	Proximal type	Proximal grade	Proximal size (cm)
1	41	M	No	1	0.9	2	T, T	L, L	1.3, 0.4
2	75	M	No	1	0.2	1	TV	L	0.8
3	59	M	Yes	1	0.2	1	T	L	1.0
4	65	F	Yes	1	0.3	1	T	H	1.0
5	70	F	Yes	2	0.6, 0.8	4	T, T, T, T	L, L, L, L	3.0, 0.5, 0.2, 0.2
6	68	F	No	1	0.5	1	T	L	1.0
7	61	M	No	1	0.8	2	T, T	L, L	0.2, 1.0
8	67	M	No	1	0.2	6	T, T, T, T, T, T	L, L, L, L, L, L	0.2, 0.2, 0.2, 0.2, 0.2, 1.3
9	66	M	No	1	0.6	6	T, T, T, T, T, T	L, L, L, L, L, H	1.0, 0.5, 0.5, 0.8, 0.5, 1.0
10	70	M	No	1	0.2	1	TV	L	1.2
11	47	M	Yes	1	0.4	1	T	L	1.4
12	50	M	Yes	1	0.5	1	T	L	1.0
13	69	M	No	3	0.5, 0.7, 0.8	6	T, T, TV, T, T, T	L, L, L, L, L, L	0.5, 1.5, 0.6, 0.8, 0.5, 0.4
14	62	M	No	1	0.5	1	TV	L	2.5
15	55	M	Yes	1	0.4	2	T, T	L, L	0.5, 2.0

T, Tubular adenoma; TV, tubulovillous adenoma; L, low-grade dysplasia; H, high-grade dysplasia.

<sup>a</sup>At least 1 first-degree relative with colorectal cancer.

distal advanced with a proximal advanced adenoma in comparison with a distal nonadvanced with a proximal advanced adenoma did not significantly change (Table 6). In each circumstance, the adjusted  $\chi^2$  test remained significant and the estimator of the common OR was similar, indicating the relationship was not altered even after adjustment for the stratifying variable (Table 6). The analysis was not different when performed in subgroups by reason for colonoscopy, whether for an abnormal barium enema or flexible sigmoidoscopy, hematochezia or positive fecal occult blood test, or for pain or other miscellaneous reasons (Table 6).

Review of the 142 patients who were excluded because of adenomas with missing information showed no differences in demographic or polyp characteristics compared with the overall sample.

Complete information was available on 288 subjects in the PPT without previous adenomas who had adenomatous polyps confined to the proximal colon. Of these subjects, 13.5% had villous changes, 3.5% had high-grade dysplasia, 17.0% had an adenoma  $\geq 1$  cm, and 24.7% had an advanced adenoma. These percentages were not significantly different from the proximal adenomas observed in patients with both distal and proximal adenomas. Because the conditional probability of a proximal adenoma in subjects without a distal adenoma

**Table 5.** Effect of Altering the Definition of What Was Considered a Distal Adenoma

Definition	No. of eligible participants <sup>a</sup>	Odds ratio <sup>b</sup>	P value	% (n) of missed advanced proximal adenomas <sup>c</sup>
Not including splenic flexure, $\leq 50$ cm <sup>d</sup>	981	2.1	0.03	36 (15/42)
Including splenic flexure, $\leq 60$ cm	1008	2.2	0.04	35 (13/37)
Not including splenic flexure, $\leq 60$ cm	993	2.1	0.03	36 (15/42)
Not including splenic flexure, $\leq 40$ cm	962	1.9	0.06	38 (17/45)
Not including descending colon, $\leq 50$ cm	872	1.9	0.05	38 (19/50)
Not including descending colon, $\leq 40$ cm	853	1.7	0.09	40 (21/53)

<sup>a</sup>Altering the definition of a distal adenoma changes the number of eligible participants by changing the number of subjects who have a distal adenoma.

<sup>b</sup>OR of the prevalence of a distal advanced adenoma associated with a proximal advanced adenoma in comparison to a distal nonadvanced adenoma associated with a proximal advanced adenoma.

<sup>c</sup>Percent of advanced proximal adenomas that would have gone undetected if a colonoscopy had not been performed for a distal nonadvanced adenoma.

<sup>d</sup>Definition used in article.

**Table 6.** Stratified Analyses by Age, Gender, and Reason for Colonoscopy

	OR <sup>a</sup> (95% CI)	P value
Age (yr)		
<60	2.7 (0.9–9.1)	
$\geq 60$	1.8 (0.7–4.4)	
CML OR <sup>b</sup>	2.1 (1.1–4.3)	0.03
Gender		
Male	1.7 (0.8–3.1)	
Female	3.7 (0.9–17.3)	
CML OR	2.1 (1.1–4.3)	0.03
Reason for colonoscopy		
After abnormal barium enema or flexible sigmoidoscopy		
Yes	1.7 (0.6–5.1)	
No	2.4 (1.0–6.2)	
CML OR	2.1 (1.1–4.3)	0.03
FOBT positive or hematochezia		
Yes	2.1 (0.7–7.1)	
No	2.1 (0.9–5.0)	
CML OR	2.1 (1.0–4.3)	0.04
Pain or other		
Yes	1.8 (0.6–5.6)	
No	2.4 (1.0–6.2)	
CML OR	2.1 (1.1–4.4)	0.03

<sup>a</sup>OR of the prevalence of a distal advanced adenoma associated with a proximal advanced adenoma in comparison to a distal nonadvanced adenoma associated with a proximal advanced adenoma.

<sup>b</sup>Conditional maximum likelihood (CML) estimator of the common OR and exact 95% CI.

was 100% in the PPT, we cannot estimate the prevalence of proximal adenomas in the absence of distal adenomas.

## Discussion

Adenomatous polyps are neoplastic precursors of colorectal cancer.<sup>3</sup> The incidence of adenomatous polyps, however, far exceeds the incidence of colorectal cancer. Although data are limited, studies suggest that individuals without advanced distal adenomas, or adenomas with villous histology, high-grade dysplasia, or  $\geq 1$  cm in size, are at average risk for colorectal cancer.<sup>27,31</sup> This engenders an important question pertinent to screening for colorectal cancer: should individuals with a nonadvanced adenoma found at screening flexible sigmoidoscopy undergo colonoscopy to determine whether they have an advanced proximal adenoma? Although numerous reports have shown about a 30% prevalence of a synchronous proximal adenoma in individuals with a distal adenoma,<sup>6–24</sup> the prevalence estimate for the presence of an advanced proximal adenoma is less certain.<sup>13,20–22</sup>

This issue is becoming increasingly important because the detection of a polypoid abnormality on screening flexible sigmoidoscopy is common and the use of screening sigmoidoscopy is likely to increase. Most studies,<sup>21,25</sup> including experience with more than 4000 screening

examinations (J. Weissfeld, personal communication, October 1997), show a 20%–25% prevalence of a polypoid abnormality on sigmoidoscopy, with some studies reporting up to a 40% positive rate.<sup>45</sup> Even if these polypoid abnormalities are sampled, and colonoscopy is limited to patients with adenomatous polyps, approximately 10%–13% of individuals undergoing screening will require a full colonoscopy.<sup>25</sup> The recent publication of several case-control studies showing a 70%–90% reduction in the risk of mortality from distal colorectal cancer with screening,<sup>46–48</sup> and the upgraded recommendation in favor of screening sigmoidoscopy by the U.S. Preventive Services Task Force, the American Cancer Society, and the Agency for Health Care and Policy Research task force, should increase practitioner and patient enthusiasm for the procedure.<sup>49</sup>

A number of experts have advocated limiting colonoscopy to individuals with advanced distal adenomas found on sigmoidoscopy.<sup>3,5,50,51</sup> Such a strategy is cost saving, but at a price, i.e., not detecting advanced lesions in the proximal colon. Limiting colonoscopy to individuals with advanced adenomas on flexible sigmoidoscopy will reduce the need for diagnostic colonoscopy after screening by an estimated 50%–70%.<sup>33,52</sup> The basis for eliminating these colonoscopies is that the yield for an advanced proximal adenoma will be small. Numerous studies show that distal adenomas are more likely to have advanced pathological features compared with adenomas in the proximal colon,<sup>53</sup> including a tendency to be larger<sup>41,44,54</sup> and more likely to manifest high-grade dysplasia.<sup>44</sup>

In this study, individuals with advanced distal adenomas were found to be two times more likely to have advanced proximal adenomas than individuals without advanced distal adenomas. This is the largest study to examine the relationship between distal and proximal adenomas. The sample is drawn from diverse geographic areas, patient and polyp characteristics were carefully documented, complete examination of the colon was required, and all polyps underwent central, independent pathological review for histology and dysplasia, which minimizes interobserver pathological variability. The prevalence of an advanced proximal adenoma in the absence of an advanced distal adenoma was 2.9%, an estimate consistent with the data from previous studies.<sup>13,20–22</sup> If the recommendations of those favoring limiting diagnostic colonoscopy to individuals with advanced distal adenomas were simulated in our population, 36% of the advanced proximal adenomas would not have been discovered.

Some health maintenance organizations recommend that individuals with more than one adenoma on flexible

sigmoidoscopy or a single adenoma between 6 and 9 mm undergo colonoscopy.<sup>32</sup> Applying these criteria to our sample would reduce the miss rate from 36% to 24% (Table 4). However, it should be noted that endoscopic estimation of polyp size, such as distinguishing a 5- from a 6-mm polyp, is difficult, often inaccurate, and may be an unreliable method on which to base clinical practice guidelines.<sup>55</sup>

Currently, there is unanimous agreement that individuals with advanced distal adenomas should undergo full colonoscopy. Our sample estimates that 5.9% of them will have an advanced proximal adenoma. Although statistically greater, the 2.9% of individuals without an advanced distal adenoma who will have an advanced proximal adenoma are in absolute terms not that appreciably different. It is difficult to strongly advise patients that they need a colonoscopy because of a 6% chance of having an additional advanced proximal lesion, but to advise otherwise comparable patients that they do not need a colonoscopy because the risk of an additional advanced proximal lesion is only 3%. It is unlikely that this magnitude of difference would be significant enough to deter a patient's decision, if given the choice, to undergo a colonoscopy.

These data pertain only to patients with a distal adenoma. The prevalence of advanced proximal adenomas in patients with no polypoid abnormalities or only a distal hyperplastic polyp, which is not a marker for a proximal adenoma,<sup>9,14</sup> cannot be answered from this data set. Although studies with screening colonoscopy<sup>23,24,56,57</sup> report a 25%–41% prevalence of isolated proximal adenomas, sufficient information on the prevalence of isolated advanced proximal adenomas is not available. Retrospective studies of patients with proximal colon cancer reveal that about 75% have no distal adenomatous lesions.<sup>58–62</sup> One study estimated that about 30% of all colorectal cancers would be missed with a negative screening sigmoidoscopy or a sigmoidoscopy that did not detect a distal adenoma.<sup>58</sup> Recent changes in the anatomic distribution of colon cancer may increase the miss rate, because some data suggest that proximal colon cancer is increasing,<sup>63</sup> possibly due to the aging of the population.<sup>54,64</sup> A more reliable estimate of the prevalence of isolated advanced proximal adenomas will be forthcoming with the completion of the Veterans Affairs screening colonoscopy study of 3000 asymptomatic patients. It will be of interest to see if the prevalence of advanced proximal adenomas in that study will vary with the presence or absence of distal adenomas.

If patients with no findings on flexible sigmoidoscopy also turn out to have about a 3% prevalence of an advanced proximal adenoma, two general approaches

could be considered. One would be to restrict colonoscopy to patients with advanced distal adenomas, since they are at higher risk, and colonoscopy is an expensive procedure. Alternatively, finding a 3% prevalence of advanced proximal adenoma in individuals with no adenomas on flexible sigmoidoscopy might indicate that everyone should undergo colonoscopy. Whether newer screening techniques such as virtual colonoscopy<sup>65,66</sup> or significant reductions in colonoscopy costs<sup>67,68</sup> will permit wider implementation of total colon examinations remain areas of active research.

The characteristics of the adenomas in our sample are consistent with previous reports. Because 47% of our participants had an advanced distal adenoma, limiting colonoscopy to those with advanced distal adenomas would have reduced the colonoscopy rate in our population by 53%, within the 50%–70% reduction estimated by others.<sup>33,52</sup> As in other studies,<sup>41,44,53,54</sup> in our sample advanced adenomas were less frequent in the proximal colon, with only 20% of our patients with proximal adenomas having an advanced adenoma.

Several limitations of this study should be emphasized. The participants were selected from a population undergoing diagnostic colonoscopy and not from individuals undergoing screening. However, several studies suggest that the prevalence of polyps is unrelated to symptoms. For example, adenoma prevalence and distribution did not differ among patients undergoing endoscopy for bleeding vs. nonbleeding symptoms.<sup>41,69,70</sup> Similarly, studies of screening colonoscopy show a similar prevalence of adenomas to studies of symptomatic patients.<sup>23,24,56,57</sup> In addition, our results were not altered after adjusting for the reason why the colonoscopy was performed (Table 6). Secondly, because this analysis was based on colonoscopy results, detection by flexible sigmoidoscopy was approximated. A study from the early 1980s estimated that sigmoidoscopy extended to only the sigmoid-descending junction<sup>71</sup>; however, the current generation of instruments may allow further depth of insertion. Regardless, expanding or shrinking the depth of insertion that defined an adenoma as distal did not alter our results. Finally, individuals with colorectal cancer were excluded from this sample. However, because only a few cancers would be expected in a sample of 1000 patients,<sup>35</sup> including prevalent cancers would not alter the conclusions.

In summary, individuals with an advanced distal adenoma are more likely to have an advanced proximal adenoma than individuals with a nonadvanced adenoma. However, eschewing a colonoscopy in patients with a nonadvanced distal adenoma would result in not detecting 36% of the advanced proximal adenomas prevalent in

patients with a distal adenoma. Whether the 3% prevalence of advanced proximal adenomas in patients with a nonadvanced distal adenoma is higher than the background prevalence in patients with no distal adenomas could not be determined from this data set.

These data can be used to support performance of a colonoscopy in patients with a nonadvanced distal adenoma found on flexible sigmoidoscopy. Further confirmation of these results in asymptomatic subjects undergoing screening sigmoidoscopy is advisable.

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## ***Charcot of Charcot's triad***



Jean Martin Charcot (1825-1893) was born in Paris and as a youth wavered in his ambition to become an artist or a physician. He chose medicine. Among his influential teachers was the famed Claude Bernard. Following graduation he was named physician to the Salpêtrière, at that time a refuge for indigent women. In its 4000 beds, Charcot found a gold mine of clinical material. His clinics, conducted with theatrical dramatics, attracted a host of students. In his eponymous legacy are Charcot's triad (biliary 'colic,' fever and chills, jaundice) indicating acute cholangitis, Charcot's joint (a neuropathic arthritis in cases of luetic tabes dorsalis), and Charcot-Leyden crystals (an eosinophilic detritus found in the sputum of chronic asthmatics and in the feces in certain cases of parasitism).

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