Sex-Specific Prevalence of Adenomas, Advanced Adenomas, and Colorectal Cancer in Individuals Undergoing Screening Colonoscopy

Monika Ferlitsch, MD
Karoline Reinhart, MD
Sibylle Pramhas, MD
Caspar Wiener, MD
Orsolya Gal, MD
Christina Bannert, MD
Michaela Hassler
Karin Kozbial
Daniela Dunkler, PhD
Michael Trauner, MD
Werner Weiss, MD

Context Although some studies have shown that men are at greater age-specific risk for advanced colorectal neoplasia than women, the age for referring patients to screening colonoscopy is independent of sex and usually recommended to be 50 years.

Objective To determine and compare the prevalence and number needed to screen (NNS) for adenomas, advanced adenomas (AAs), and colorectal carcinomas (CRCs) for different age groups in men and women.

Design, Setting, and Patients Cohort study of 44 350 participants in a national screening colonoscopy program over a 4-year period (2007 to 2010) in Austria.

Main Outcome Measures Prevalence and NNS of adenomas, AAs, and CRCs in different age groups for men and women.

Results The median ages were 60.7 years (interquartile range [IQR], 54.5-67.5 years) for women and 60.6 years (IQR, 54.3-67.6 years) for men, and the sex ratio was nearly identical (51.0% [22 598] vs 49.0% [21 572]). Adenomas were found in 19.7% of individuals screened (95% CI, 19.3%-20.1%; n=8743), AAs in 6.3% (95% CI, 6.1%-6.5%; n=2781), and CRCs in 1.1% (95% CI, 1.0%-1.2%; n=491); NNS were 5.1 (95% CI, 5.0-5.2), 15.9 (95% CI, 15.4-16.5), and 90.9 (95% CI, 83.3-100.0), respectively. Male sex was significantly associated with a higher prevalence of adenomas (24.9% [95% CI, 24.3%-25.4%] vs 14.8% [95% CI, 14.3%-15.2%]; $P<.001$; unadjusted odds ratio [OR], 1.9 [95% CI, 1.8-2.0]), AAs (8.0% [95% CI, 7.6%-8.3%] vs 4.7% [95% CI, 4.4%-4.9%]; $P<.001$; unadjusted OR, 1.8 [95% CI, 1.6-1.9]), and CRCs (1.5% [95% CI, 1.3%-1.7%] vs 0.7% [95% CI, 0.6%-0.9%]; $P<.001$; unadjusted OR, 2.1 [95% CI, 1.7-2.5]). The prevalence of AAs in 50- to 54-year-old individuals was 5.0% (95% CI, 4.4%-5.6%) in men but 2.9% (95% CI, 2.5%-3.4%) in women (adjusted $P=.001$); the NNS in men was 20 (95% CI, 17.8-22.6) vs 34 in women (95% CI, 29.1-40; adjusted $P=.001$). There was no statistical significance between the prevalence and NNS of AAs in men aged 45 to 49 years compared with women aged 55 to 59 years (3.8% [95% CI, 2.3%-6.1%] vs 3.9% [95% CI, 3.3%-4.5%] and 26.1 [95% CI, 16.5-44.4] vs 26 [95% CI, 22.5-30.2]; $P=.99$).

Conclusion Among a cohort of Austrian individuals undergoing screening colonoscopy, the prevalence and NNS of AAs were comparable between men aged 45 to 49 years and women aged 55 to 59 years.

JAMA. 2011;306(12):1352-1358 www.jama.com

As in many countries, including the United States, the recommended age in Austria for screening colonoscopy for colorectal cancer (CRC) in average-risk patients is 50 years for both men and women[1-4] because of the increase in the prevalence of CRC in the sixth decade of life. The goal of screening colonoscopy is to find and remove adenomas and particularly advanced adenomas (AAs). Although transition rates from AA to CRC are similar for women and men, the prevalences of AA and CRC are higher in men than in women (8% vs 4.3% for AA, 1.4% vs 0.6% for CRC, respectively),[5-8] which may result from a larger number of adenomas present in men in their 40s.[7] Based on the results of a national screening program in Poland, Regula et al[5] have suggested that the age for starting screening colonoscopy should be sex specific,

Author Affiliations: Quality Assurance Working Group, Austrian Society for Gastroenterology and Hepatology, Vienna, Austria (Drs Ferlitsch, Reinhart, Pramhas, Wiener, Gal, Bannert, and Weiss and Ms Hassler); Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna (Drs Ferlitsch, Reinhart, Pramhas, Wiener, Gal, Bannert, and Trauner and Ms Kozbial); and Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna (Dr Dunkler).
Corresponding Author: Monika Ferlitsch, MD, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Waehringer Guertel 18-20, Vienna A-1090, Austria (monika.ferlitsch@meduniwien.ac.at).

 ©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

because the number needed to screen (NNS) to detect an AA among men aged 40 to 49 years was similar to that of women aged 50 to 59 years. A study by Brenner et al[6] revealed that the same incidence of CRC and CRC mortality occurred in women 4 to 8 years later than in men, but the patients included in this study were 55 years or older. Nevertheless, a modification of the screening recommendations because of sex has not been implemented because the optimal age for screening has remained insufficiently explored.

In 2007, a national project entitled Quality Management for Colon Cancer Prevention was initiated to define and control standards for quality and documentation of screening colonoscopies in Austria. The objective of our study was to investigate the most appropriate age for initial screening colonoscopy for both male and female patient groups to achieve a higher detection rate of adenoma, AA, and CRC, which could result in a lower CRC mortality rate.

METHODS

Colonoscopy as a screening method was established in Austria in 2005. Because of the lack of standardized guidelines for the quality of screening colonoscopy within Austria (with different quality standards and reimbursement policies for colonoscopies in each of the 9 federal states), the Austrian Society of Gastroenterology and Hepatology (OEGGH), together with the Austrian Federation of the Statutory Insurance Institutions and the Austrian Cancer Aid, launched a large national project called the Certificate of Quality for Screening Colonoscopy in 2007.

Experienced endoscopists in practices and hospitals (ie, board-certified specialists for internal medicine or surgery) can apply for this certificate if they conform to the quality standards of the OEGGH, including guidelines about information and consultation, premedication, video colonoscopy, cecal intubation rates (>85%), documentation, physician qualification (eg, polypectomy skills), emergency equipment and experience, endoscope reprocessing, and microbiological controls. Qualified physicians must have conducted at least 200 colonoscopies and 50 polypectomies under supervision and independently performed 100 colonoscopies and at least 10 polypectomies per year.

Study Procedure

Two hundred twenty-five endoscopic units (44.8% of Austrian colonoscopists,[9] 142 private practices, 81 endoscopic units in hospitals, and 2 outpatient clinics) applied for the OEGGH quality certificate and participated in our study.

Data were provided from 44 350 screening colonoscopies (representing 1.68% of overall Austrian population aged 50-79 years) performed between November 2007 and December 2010. Patients were referred for screening by physicians and not directly solicited. Patients were eligible if they were aged 50 to 100 years. We also received data from younger individuals (aged 30-49 years) if the colonoscopy had "screening characteristics": ie, asymptomatic patients who were screened because of a positive family history or patients who reported fear of colon cancer. Separate written informed consent was obtained from each patient for the colonoscopy and for providing data to the OEGGH. The study was approved by the Austrian data protection committee.

The participating centers and physicians were advised to provide data only from screening colonoscopies. Each participating physician was required to store data from the colonoscopy and histopathological analysis and video or photographic documentation in case of data monitoring by the OEGGH. The original colonoscopy documentation, including the indication screening and photographic documentation, was inspected annually from 3 random samples in each participating center or physician.

All data, including colonoscopy results and histopathological analyses, were recorded and transferred to the study database using an electronically signed web form along with the patient medical records. All histopathological analyses were performed by board-certified pathologists trained in gastrointestinal pathology.

Histological findings were categorized according to the most advanced lesion identified. Adenomas were considered advanced if they had high-grade dysplasia, villous or tubulovillous histologic characteristics, or any combination thereof or if they were tubular adenomas at least 10 mm in diameter.

Statistical Analysis

Patient characteristics are described with median values and interquartile ranges (IQRs) for nonnormally distributed variables and with frequencies and percentages for categorical variables. We used Mann-Whitney U tests, χ^2 tests, or Fisher exact tests to compare these characteristics between men and women. For ease of interpretation, we defined age groups by 5-year periods starting at age 30 years. However, because of screening colonoscopy referral guidelines, few patients were younger than 50 years. 95% CIs are given to estimate the uncertainty due to small numbers of patients. When the same analysis was repeated for different age groups, a step-down Bonferroni correction for multiple testing was applied, for which we report adjusted *P* values.

Prevalence, NNS, odds ratios (ORs), and corresponding 95% CIs for men and women were computed. For prevalence and NNS, exact CIs were used. We used logistic regression to model the association of detection of adenoma, AA, or CRC. Our primary interest was potential differences between men and women with respect to age. Therefore, we included sex and continuous age in the regression model. For all 3 models, we tested for an interaction between age and sex. No significant

©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

interaction was found between age and sex (adenoma $P=.98$, AA $P=.38$, and CRC $P=.36$). No missing values were found. For all hypothesis tests, we considered $P<.05$ statistically significant, and all tests were 2-sided. All statistical computations were performed with SAS version 9.2 (SAS Institute, Cary, North Carolina). The graphic was produced with R (http://www.r-project.org).

Table 1. Patient Characteristics

	No. (%)			*P* Value, Women vs Men
	All	Women	Men	
Patients, No.	44 350	22 598 (51.0)	21 752 (49.0)	
Age range, y	30.0-97.1	30.0-94.9	30.1-97.1	
Median (IQR), y	60.7 (54.4-67.5)	60.7 (54.5-67.5)	60.6 (54.3-67.6)	.12
Age groups, y				
30-34	115 (0.3)	59	56	
35-39	203 (0.5)	105	98	
40-44	466 (1.0)	236	230	
45-49	846 (1.9)	403	443	
50-54	10 533 (23.8)	5271	5262	
55-59	8793 (19.8)	4519	4274	
60-64	8239 (18.6)	4319	3920	
65-69	7890 (17.8)	4006	3884	
70-74	4080 (9.2)	2031	2049	
75-79	2199 (5.0)	1153	1046	
80-84	803 (1.8)	394	409	
85-89	167 (0.4)	94	73	
90-94	14 (>0.1)	8	6	
>94	2 (>0.1)	0	2	
Sedation used	38 474 (86.8)	20 571 (91)	17 903 (82.3)	<.001
Cecal intubation	42 414 (95.6)	21 407 (94.7)	21 007 (96.6)	<.001
Reasons for no cecal intubation				
Pain	516 (26.7)	358 (30.1)	158 (21.3)	
Poor bowel preparation	384 (20.9)	229 (19.2)	155 (20.9)	
Stenosis	232 (12)	135 (11.3)	97 (13.1)	
Complication	45 (2.3)	28 (2.4)	17 (2.3)	
Others	756 (39.1)	441 (37)	315 (42.4)	
Complication	111 (0.26)	48 (0.11)	63 (0.15)	<.001
Cardiopulmonary	46 (41.44)	30 (62.5)	16 (25.4)	
Bleeding	54 (48.65)	15 (31.25)	39 (61.9)	
Perforation	3 (2.70)	1 (2.08)	2 (3.17)	
Other	8 (7.21)	2 (4.17)	6 (9.52)	
Form of polyps				
Flat	3826 (24.7)	1669 (25.8)	2157 (24)	<.001
Sessile	9550 (61.8)	4023 (62.1)	5527 (61.5)	
Pedunculated	2086 (13.5)	783 (12.1)	1303 (14.5)	
Polyp count	15 267 (34.4)	6398 (28.3)	8869 (40.8)	<.001
0	28 896			
1	8511 (55.1)	3866 (59.7)	4645 (51.7)	
2-4	5929 (38.4)	2258 (34.9)	3671 (40.9)	
>4	1014 (6.6)	349 (5.4)	665 (7.4)	
Polyp size, mm				
<5	9310 (60.3)	4025 (62.3)	5285 (58.8)	<.001
5-10	4503 (29.2)	1797 (27.8)	2706 (30.1)	
11-20	1164 (7.5)	482 (7.5)	682 (7.6)	
>20	473 (3.1)	162 (2.5)	311 (3.5)	
Polyp location				
Only sigmoid colon/rectum	8510 (55.03)	3795 (58.6)	4715 (52.5)	<.001
Proximal to sigmoid colon	3163 (20.5)	1325 (20.5)	1838 (20.5)	
Proximal and distal colon	3792 (24.5)	1356 (20.9)	2436 (27.1)	

Abbreviation: IQR, interquartile range.

RESULTS

A total of 44 350 patients—22 598 women (51.0%) and 21 752 men (49.0%)—underwent screening colonoscopy at Austrian endoscopy units in the quality certificate program from November 2007 to December 2010 (TABLE 1). The median ages were 60.7 years (IQR, 54.5-67.5 years) for women and 60.6 years (IQR, 54.3-67.6 years) for men.

Sedation, Cecal Intubation, and Complications

Sedation (midazolam or propofol or a combination) was used during 86.8% (n=38 474) of the colonoscopies. The cecum was reached in 95.6% (n=42 414) of the patients. Clinically relevant complications occurred in 111 patients (0.3%) and included 3 perforations during polypectomy with snare. No deaths were registered as a result of screening colonoscopy or its complications. Women had lower rates of complications than men (0.11% [48] vs 0.15% [63]; $P<.001$) (Table 1). Cardiopulmonary events were twice as common in women ($P<.001$) because of higher sedation rates in women compared with men. Bleeding occurred more frequently in men ($P<.001$). Cardiopulmonary complications increased with age—from 0.05% in 50- to 60-year-old patients to 0.25% in 70- to 80-year-old patients ($P<.001$)—whereas bleeding complications remained unchanged ($P=.23$).

Screening Results

Findings included polyps in 34.4% (n=15 267), colon cancer in 0.4% (n=162), rectal cancer in 0.2% (n=92), and other issues in 3.6% (n=1600). In 61.4% (n=27 212) of the colonoscopies, no abnormalities were found. The percentage of each macroscopic finding was higher in men than women. In colonoscopies in which polyps were de-

©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

tected, polyps were detected only in the proximal colon in 20.5% (n=3163), in the sigmoid colon or rectum in 55% (n=8510), and in the distal and proximal colon in 24.5% (n=3792). Polypectomy was performed for 12 215 individuals (94.6%) during the screening colonoscopy. It was performed with a forceps in 70.3%, with a snare in 15.5%, and with both in 8.8%. The numbers, sizes, and shapes of the polyps differed between male and female patients (Table 1).

Histological Findings

The histological analysis revealed 16.3% of patients (n=7231) had hyperplastic polyps, 19.7% (n=8743) had adenomas, 0.5% (n=217) had high-grade intraepithelial neoplasia, 1.1% (95% CI, 1.0%-1.2%; n=491) had carcinoma, and 2% (n=889) had other abnormalities. Hyperplastic polyps were found in 18.3% (n=3990) of male and 14.3% (n=3241) of female patients ($P<.001$), adenomas in 24.9% (n=5407) of male and 14.8% (n=3336) of female patients ($P<.001$), high-grade intraepithelial neoplasia in 0.7% (n=147) of male and 0.3% (n=70) of female patients ($P<.001$), and carcinoma in 1.5% (n=326) of male vs 0.7% (n=165) of female patients ($P<.001$).

Of the 19.7% (95% CI, 19.3%-20.1%; n=8743) adenomas found, 6.27% (95% CI, 6.1%-6.5%; n=2781) were classified as advanced (AAs); 70.5% (n=1960) of these had tubulovillous characteristics, 19.6% (n=546) had tubular characteristics and a size greater than 1 cm, 7.8% (n=217) had high-grade dysplasia, and 2.1% (n=58) had villous histological characteristics. There were no differences by sex in histological findings for AA ($P=.37$).

Prevalence and NNS for Adenoma

The prevalence of adenomas was 24.9% (95% CI, 24.3%-25.4%) for men and 14.8% (14.3%-15.2%) for women ($P<.001$) (TABLE 2). Comparing the prevalence between men and women, the unadjusted OR was 1.9 (95% CI, 1.8-2.0; $P<.001$). The prevalence of adenomas among 50- to 54-year-old men was 18.5% (95% CI, 17.5%-19.6%), which was greater than the prevalence among women in the same age group (10.7% [95% CI, 9.9%-11.6%]; adjusted $P=.001$) but similar to the preva-

Table 2. Prevalence and Number Needed to Screen to Detect Adenoma, Advanced Adenoma, and Colorectal Carcinoma Among Different Age Groups of Women and Men[a]

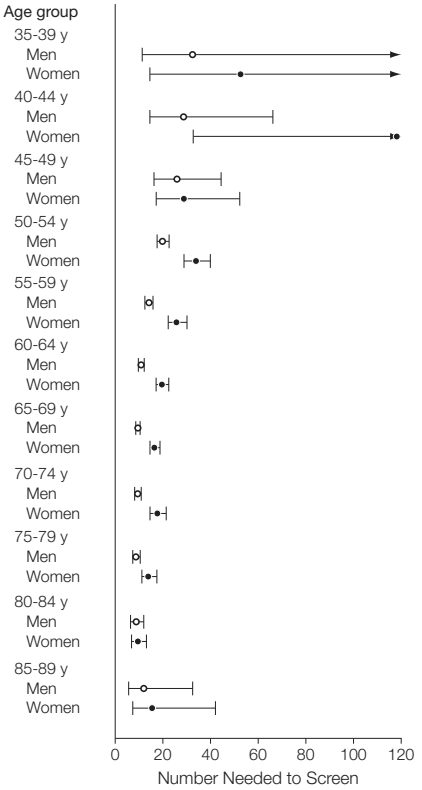
	Women		Men	
	Prevalence, No. (%) [95% CI]	NNS [95% CI]	Prevalence, No. (%) [95% CI]	NNS [95% CI]
		Adenoma		
All	3336 (14.8) [14.3-15.2]	6.7 [6.6-7.0]	5407 (24.9) [24.3-25.4]	4.0 [3.9-4.1]
Age, y				
30-34	1 (1.7) [0.04-9.1]	59.0 [11.0-2330.9]	2 (3.6) [0.4-12.3]	28.0 [8.1-229.6]
35-39	5 (4.8) [1.6-10.8]	21.0 [9.3-63.9]	5 (5.1) [1.7-11.5]	19.6 [8.7-59.6]
40-44	17 (7.2) [4.25-11.3]	13.9 [8.9-23.5]	28 (12.2) [8.2-17.1]	8.2 [5.8-12.1]
45-49	41 (10.2) [7.4-13.6]	9.8 [7.4-13.5]	75 (16.9) [13.6-20.1]	5.9 [4.8-7.4]
50-54	564 (10.7) [9.9-11.6]	9.3 [8.6-10.1]	975 (18.5) [17.5-19.6]	5.4 [5.1-5.7]
55-59	592 (13.2) [12.1-14.1]	7.6 [7.1-8.2]	984 (23.0) [21.8-24.3]	4.3 [4.1-4.6]
60-64	714 (16.5) [15.4-17.7]	6.0 [5.7-6.5]	1057 (27.0) [25.6-28.4]	3.7 [3.5-3.9]
65-69	716 (17.9) [16.7-19.1]	5.6 [5.2-6.0]	1149 (29.6) [28.2-31.1]	3.4 [3.2-3.6]
70-74	373 (18.4) [16.7-20.1]	5.4 [5.0-6.0]	656 (32.0) [30-34]	3.1 [2.9-3.3]
75-79	212 (18.4) [16.2-20.8]	5.4 [4.9-6.2]	326 (31.2) [28.4-34.1]	3.2 [2.9-3.5]
80-84	84 (21.3) [17.4-25.7]	4.7 [3.9-5.8]	130 (31.8) [27.3-36.5]	3.1 [2.7-3.7]
85-89	16 (17) [10.1-26.2]	5.9 [3.8-10.0]	18 (24.7) [15.3-36.1]	4.1 [2.8-6.5]
90-94	1 (12.5) [0.3-52.7]		1 (16.7) [0.4-64.1]	6.0 [1.6-237.5]
		Advanced Adenoma		
All	1050 (4.65) [4.4-4.9]	21.5 [20.3-22.8]	1731 (7.96) [7.6-8.3]	12.6 [12.0-13.2]
Age, y				
30-34	0	No NNS	0	No NNS
35-39	2 (1.9) [0.2-6.7]	52.5 [14.9-431.9]	3 (3.1) [0.6-8.7]	32.7 [11.5-157.3]
40-44	2 (0.9) [0.1-3]	118.0 [33.0-972.8]	8 (3.5) [1.5-6.7]	28.7 [14.8-66.1]
45-49	14 (3.5) [1.5-5.8]	28.8 [17.4-52.3]	17 (3.8) [2.3-6.1]	26.1 [16.5-44.4]
50-54	155 (2.9) [2.5-3.4]	34.0 [29.1-40.0]	263 (5.0) [4.4-5.6]	20.0 [17.8-22.6]
55-59	174 (3.9) [3.3-4.5]	26.0 [22.5-30.2]	301 (7.0) [6.3-7.9]	14.2 [12.7-15.9]
60-64	219 (5.1) [4.4-5.8]	19.7 [17.3-22.5]	355 (9.0) [8.2-10]	11.0 [10.0-12.2]
65-69	241 (6.0) [5.3-6.8]	16.6 [14.7-18.9]	401 (10.3) [9.4-11.3]	9.7 [8.8-10.7]
70-74	114 (5.6) [4.7-6.7]	17.8 [14.9-21.5]	212 (10.4) [9.1-11.8]	9.7 [8.5-11.0]
75-79	82 (7.1) [5.7-8.8]	14.1 [11.4-17.6]	118 (11.3) [9.4-13.4]	8.9 [7.5-10.6]
80-84	41 (10.4) [7.6-13.9]	9.6 [7.2-13.2]	46 (11.3) [8.4-14.7]	8.9 [6.8-12.0]
85-89	6 (6.4) [2.4-13.4]	15.7 [7.5-42.0]	6 (8.2) [3.1-17]	12.2 [5.9-32.5]
90-94	0	No NNS	1 (16.7) [0.4-64.1]	6.0 [1.6-237.5]
		Colorectal Carcinoma		
All	165 (0.7) [0.62-0.85]	137.0 [117.7-160.4]	326 (1.5) [1.3-1.7]	66.7 [60.0-74.6]
Age, y				
30-34	0	No NNS	1 (1.8) [0.1-9.6]	56.0 [10.5-2212.4]
35-39	1 (1.0) [0.02-5.2]	105.0 [19.3-4147.8]	1 (1.0) [0.03-5.6]	98.0 [18.0-3871.3]
40-44	1 (0.4) [0.01-2.3]	236.0 [42.8-9322.0]	1 (0.4) [0.01-2.4]	230.0 [41.7-9085]
45-49	1 (0.2) [0.01-1.4]	403.0 [72.7-15 918.2]	5 (1.1) [0.4-2.6]	88.6 [38.3-272.1]
50-54	20 (0.4) [0.2-0.6]	263.6 [170.8-431.2]	42 (0.8) [0.6-1.1]	125.3 [92.8-173.6]
55-59	26 (0.6) [0.4-0.8]	173.8 [118.8-265.8]	57 (1.3) [1-1.7]	75.0 [58.0-98.9]
60-64	32 (0.7) [0.5-1]	135.0 [95.8-197.1]	52 (1.3) [1-1.7]	75.4 [57.6-100.8]
65-69	49 (1.2) [0.9-1.6]	81.8 [62.0-110.4]	72 (1.9) [1.5-2.3]	53.9 [42.9-68.8]
70-74	15 (0.7) [0.4-1.2]	135.4 [82.3-241.6]	39 (1.9) [1.4-2.6]	52.5 [38.6-73.7]
75-79	13 (1.1) [0.3-2.6]	88.7 [52.1-166.2]	33 (3.2) [2.2-4.4]	31.7 [22.7-45.8]
80-84	4 (1.0) [0.3-2.6]	98.5 [38.8-360.6]	16 (3.9) [2.3-6.3]	25.6 [15.9-44.4]
85-89	2 (2.1) [0.3-7.5]	47.0 [13.4-386.5]	6 (8.2) [3.1-17]	12.2 [5.9-32.5]
90-94	1 (12.5) [0.3-52.7]	8.0 [1.9-316.5]	1 (16.7) [0.4-64.1]	6.0 [1.6-237.5]

Abbreviation: NNS, number needed to screen.
[a] $P<.001$ for adenoma, advanced adenomas, and colorectal carcinoma.

©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

Figure. Number Needed to Screen to Detect Advanced Adenomas in Men and Women



Error bars indicate 95% CIs. 95% CIs for data for patients younger than 45 years are truncated at a number needed to screen of 120. For complete 95% CI data, refer to Table 2.

lence among 65- to 69-year-old women (17.9% [95% CI, 16.7%-19.1%]).

The mean NNS to detect adenomas were 5.1 (95% CI, 5.0-5.2) for all individuals, 4.0 (95% CI, 3.9-4.1) for men, and 6.7 (95% CI, 6.6-7.0) for women ($P<.001$). In 50- to 54-year-old women, NNS was nearly twice as high as in men at the same age (9.3 [95% CI, 8.6-10.1] vs 5.4 [95% CI, 5.1-5.7]; adjusted $P=.001$). Among 45- to 49-year-old men, NNS was 5.9 (95% CI, 4.8-7.4); a similar NNS of 6.0 (95% CI, 5.7-6.5) was found for women aged 60 to 64 years.

Prevalence and NNS for AA

The prevalence of AA in men was nearly twice as high as in women (8.0% [95% CI, 7.6%-8.3%] vs 4.7% [95% CI, 4.4%-4.9%]; $P<.001$). Men had a significantly higher risk of detecting AA compared with women (unadjusted OR, 1.8; 95% CI, 1.6-1.9; $P<.001$). The prevalence of AA among 50- to 54-year-old men differed from women in the same age group (5.0% [95% CI, 4.4%-5.6%] vs 2.9% [95% CI, 2.5%-3.4%]; adjusted $P=.001$). A comparable prevalence occurred in women 10 years older, in 60- to 64-year-old women (5.1% [95% CI, 4.4%-5.8%]). The 45- to 49-year-old men had similar prevalence of AA as 55- to 59-year-old women (3.8% [95% CI, 2.3%-6.1%] and 3.9% [95% CI, 3.3%-4.5%], respectively).

The NNS to find an AA were 15.9 (95% CI, 15.4-16.5) for all individuals, 21.5 (95% CI, 20.3-22.8) for women, and 12.6 (95% CI, 12-13.2; $P<.001$) for men (FIGURE). In 50- to 54-year-old women, it was 34 (95% CI, 29.1-40) vs 20 (95% CI, 17.8-22.6) for men (adjusted $P=.001$). Men aged 45 to 49 years had a similar NNS as 55- to 59-year-old women (26.1 [95% CI, 16.5-44.4] vs 26 [95% CI, 22.5-30.2]; $P=.99$).

Prevalence and NNS for CRC

Men had a 2-fold higher risk of CRC (unadjusted OR, 2.1; 95% CI, 1.7-2.5; $P<.001$). The prevalence of CRC was twice as high among men compared with women (1.5% [95% CI, 1.3%-1.7%] vs 0.7% [95% CI, 0.6%-0.9%]; $P<.001$). A prevalence of 1.2% (95% CI, 0.9%-1.6%) among 65- to 69-year-old women was similar to that in 55- to 59-year-old men (1.3% [95% CI, 1.0%-1.7%]). An increase in the prevalence of CRC was detected in women aged 65 to 69 years and in men who were 10 years younger (ie, aged 55-59 years).

Mean NNS for CRC were 90.9 (95% CI, 83.3-100.0) colonoscopies for all individuals, 66.7 (95% CI, 60-74.6) colonoscopies for men, and 137.0 (95% CI, 117.7-160.4) for women ($P<.001$). Accordingly, 55- to 59-year-old men had similar NNS for CRC to that for women who were 10 years older (65-69 years): 75.0 (95% CI, 58.0-98.9) vs 81.8 (95% CI, 62.0-110.4), respectively.

COMMENT

In our study, analysis of age- and sex-specific prevalence of adenomas, AAs, and CRC indicates a significantly higher rate of these lesions among men compared with women in all age groups, suggesting that male sex constitutes an independent risk factor for colorectal carcinoma[5,6,10-16] and indicating new sex-specific age recommendations for screening colonoscopy.

An increase in the prevalence of adenomas was seen among women aged 60 to 64 years (from 13.2% among those aged 55-59 years to 16.5% in those aged 60-64 years). A similar increase from 12.2% to 16.9% was observed among men 15 years younger, ie, 45- to 49-year-old men, comparable with results from a study by Rundle et al.[7]

Accordingly, an increase in the prevalence of AAs among women occurred at ages 55 to 59 years (from 2.9% to 3.9%), whereas a similar prevalence of AA was observed among men aged 45 to 49 years (3.8%), ie, 10 years younger, consistent with other studies.[5,6,15]

Consequently, a difference between men and women was also observed in the increased prevalence of CRC that occurred 10 years later than the increase in AAs: from 0.7% to 1.2% among women aged 65 to 69 years and a comparable increase from 0.8% to 1.3% among men aged 55 to 59 years. In adenoma detection, comparable prevalence rates were found in men aged 45 years and women who are 10 years older. The same was true for the detection of AA. In detection of CRC, 55-year-old men had comparable prevalence with 65-year-old women.

The time span from the appearance of the first abnormality to a possible malignant lesion is approximately 10 years.[17] Brenner et al[8] showed that the risk of transition from AAs to CRC was comparable among women and men but increased with age. The increased number of CRCs diagnosed at age 50 to 59 years may reflect a transition from adenomas that were present in individuals in their 40s.[7] Regula et al[5] suggested that a practical approach might be to recommend

 ©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

screening only in groups with NNS below a certain threshold. The NNS for adenoma, AAs, and CRC in our study were 5.4 (95% CI, 5.1-5.7), 20.0 (95% CI, 17.8-22.6), and 125.3 (95% CI, 92.8-173.6) in 50-to 54-year-old men, respectively, as compared with 9.3 (95% CI, 8.6-10.1), 34.0 (95% CI, 29.1-40), and 263.6 (95% CI, 170.8-431.2) for women of the same age, respectively.

The ages at which women reached a similar NNS to 50- to 54-year-old men were 60 to 64 years for both adenomas and AAs and 65 to 69 years for CRC. A comparable difference of 10 years in the NNS between the age groups of male and female participants has also been observed in other studies. Nguyen et al[10] compared the NNS of 3 studies for AA, which were 21, 17, and 10 for men aged 50 to 54 years compared with 66, 28, and 50 for women of the same age. The ages at which women reached a similar NNS to 50- to 54-year-old men in these 3 studies were 60 to 64 years, 60 to 66 years, and 65 to 75 years, respectively. Our data are consistent with those reported by the studies mentioned.[5,7,8,10]

Most national guidelines recommend that screening programs for CRC start by age 50 years for both men and women of average risk, because the risk of CRC increases in the sixth decade of life.[4,7,18] This assumption does not seem valid for both sexes because it has been observed that sex differences in the epidemiology of CRC have increased during the last few decades.[6] There is considerable evidence that CRC incidence and mortality are higher in men than in women, and an age difference of approximately 4 to 8 years is when levels of risk are comparable.[6,7,10,18]

The choice to start screening in Austria at age 50 years is based on the increase of CRC prevalence at 60 years. In data from Statistics Austria,[19] CRC incidence and mortality are twice as high in men than in women. Therefore, our data may be useful for deferring age-specific screening recommendations. It may be important to start CRC screening in men earlier than age 50 years to avoid higher prevalence in men.

Nevertheless, deciding whether to adjust the age at which screening begins also requires considering whether the recommended age for women should be older or the recommended age for men younger. Sung et al[18] suggested in the Asia Pacific consensus recommendations for colorectal cancer screening that women may start screening at later ages because of relatively low incidence of CRC at ages 50 to 55 years. Brenner et al[6] suggested that the optimal age for screening initiation be 5 years older for women than for men but recommended keeping open both options, decreasing or increasing the age. Regula et al[5] suggested recommending screening only in groups with NNS that are below a certain threshold, such as men aged 40 to 49 years with family history and women aged 50 to 59 years without family history, or men aged 50 years and women aged 60 years, since these groups had similar NNS. Furthermore, an unresolved challenge is determining the ideal NNS to find an AA in a screening population. For AA, we propose an NNS of 26 for both men and woman, which is not very high.

Further, a recent study by Atkin et al[20] showed that flexible sigmoidoscopy is a safe and practical test that, when offered only once between ages 55 and 64 years, results in substantial and lasting benefit. In our study, 55% of polyps were found in the sigmoid colon or rectum and 45% proximal to the sigmoid colon or in both parts of colon. Approximately 50% of polyps would not be detected if only sigmoidoscopy were used for screening purposes. Therefore, our data support the importance of complete colonoscopy to cecum as a screening tool to find and remove all adenomas and AAs.

Strengths of the current study include a large number of participants as well as an equal proportion of men and women in contrast to other studies where women outnumbered men[5,11] or vice versa.[7,12,13,16] Furthermore, screening in Austria begins at the age of 50 years, and we have a substantial proportion of data from younger patients, permitting an analysis of the differential risk for CRC as well as for adenomas and AAs, which seem to be the most appropriate target in CRC screening. A further strength is that all colonoscopies were performed according to a general quality guideline, thus providing comparable data about adenomas, AAs, and CRC.

However, several limitations have to be acknowledged. First, our study included only age and sex but no other confounding factors, such as family history, obesity, or smoking status. Nevertheless, Brenner at al[6] suggested that appropriate differentiation of age at initiation of CRC screening by sex might be similarly or more relevant from a public health point of view than the widely practiced differentiation by family history. A recent study by Hoffmeister et al[21] corroborated this assumption showing that male sex and smoking have a larger effect on prevalence of colorectal neoplasia than family history, suggesting an extensive evaluation of additional risk stratification in population-based screening, particularly by sex. Second, only a small number of patients (n=1630, or 3.7%) in our study were younger than 50 years, which may bias our results on NNS and AA in men aged 45 to 49 years. On the other hand, these results are further supported by the increase in prevalence of CRC in men aged 55 to 59 years and women aged 65 to 69 years. According to the adenoma carcinoma sequence, an increase in prevalence of CRC occurs 10 years later than the increase in prevalence of adenoma and AA, ie, at ages 55 to 59 years for men and 65 to 69 years for women. We therefore suggest there was no significant bias for individuals younger than 50 years. Third, data were provided from participants of a nationwide screening colonoscopy quality program that was restricted to asymptomatic patients because of strict reimbursement policies. We cannot ex-

©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

clude with confidence that a small number of patients may have been symptomatic in such a screening setting (underreporting symptoms), but we do not think that this may have skewed our data.

The American College of Gastroenterology recommends that screening in African American individuals begin at age 45 years because of an increased incidence of CRC, development at younger age, and consecutively higher mortality in comparison with white individuals.[22] Accordingly, the detection rates of polyps larger than 9 mm were 24% higher in African American individuals compared with white individuals (7.7% vs 6.2%).[23] In our study, the detection rate of AA was 71% higher in men compared with women (7.96% vs 4.65%). Therefore, new screening recommendations concerning age should be reconsidered. Further prospective studies are needed to demonstrate the relative clinical effectiveness of screening at different ages.

Author Contributions: Dr Ferlitsch had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Ferlitsch, Pramhas, Trauner, Weiss.
Acquisition of data: Ferlitsch, Reinhart, Pramhas, Wiener, Gal, Bannert, Hassler, Kozbial.
Analysis and interpretation of data: Ferlitsch, Dunkler, Trauner.
Drafting of the manuscript: Ferlitsch, Dunkler, Trauner.
Critical revision of the manuscript for important intellectual content: Ferlitsch, Reinhart, Pramhas, Wiener, Gal, Bannert, Hassler, Kozbial, Dunkler, Trauner, Weiss.
Statistical analysis: Dunkler.
Obtained funding: Reinhart, Pramhas, Wiener, Gal, Bannert, Hassler.
Administrative, technical, or material support: Reinhart, Pramhas, Wiener, Gal, Bannert, Hassler, Kozbial, Trauner.
Study supervision: Ferlitsch, Weiss.
Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
Funding/Support: The Quality Certificate for Screening Colonoscopy project was conducted in cooperation with the Main Association of Austrian Social Security Institutions and funded by the Fund for Preventive Check-ups and Health Promotion (fund § 447h ASVG).
Role of the Sponsor: The funding organizations had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.
Additional Contributions: We thank Wolfgang Vogel, MD, Department of Gastroenterology and Hepatology, Medical University of Innsbruck, Austria; Friedrich Renner, MD, Department of Internal Medicine, Krankenhaus der Barmherzigen Schwestern Ried/Innkreis, Austria; and Peter Knoflach, MD, Department of Internal Medicine I, Klinikum Wels, Wels, Austria, and the Austrian Society of Gastroenterology and Hepatology (OEGGH), for their support in the realization of this Austria-wide project and for proofreading. We thank Sabine Stowasser, DrJur, and Elisabeth Fasching, Mag(FH), Main Association of Austrian Social Security Institutions, Vienna, Austria, for their support in the organization. We thank all participants of the project for their support and data input. No one received compensation for the contributions.

REFERENCES

1. US Preventive Services Task Force. Screening for colorectal cancer: recommendation and rationale. *Ann Intern Med*. 2002;137(2):129-131.
2. Winawer S, Fletcher R, Rex D, et al; Gastrointestinal Consortium Panel. Colorectal cancer screening and surveillance: clinical guidelines and rationale: update based on new evidence. *Gastroenterology*. 2003; 124(2):544-560.
3. Smith RA, Cokkinides V, Eyre HJ; American Cancer Society. American Cancer Society guidelines for the early detection of cancer, 2004. *CA Cancer J Clin*. 2004;54(1):41-52.
4. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology*. 2008;134(5):1570-1595.
5. Regula J, Rupinski M, Kraszewska E, et al. Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. *N Engl J Med*. 2006;355 (18):1863-1872.
6. Brenner H, Hoffmeister M, Arndt V, Haug U. Gender differences in colorectal cancer: implications for age at initiation of screening. *Br J Cancer*. 2007; 96(5):828-831.
7. Rundle AG, Lebwohl B, Vogel R, Levine S, Neugut AI. Colonoscopic screening in average-risk individuals ages 40 to 49 vs 50 to 59 years. *Gastroenterology*. 2008;134(5):1311-1315.
8. Brenner H, Hoffmeister M, Stegmaier C, Brenner G, Altenhofen L, Haug U. Risk of progression of advanced adenomas to colorectal cancer by age and sex: estimates based on 840,149 screening colonoscopies. *Gut*. 2007;56(11):1585-1589.
9. Weiss W, Homoncik M. Colorectal carcinoma in Austria: update 2008 [in German]. *Journal für Gastroenterologische und Hepatologische Erkrankungen*. 2008;6(2):19-22.
10. Nguyen SP, Bent S, Chen YH, Terdiman JP. Gender as a risk factor for advanced neoplasia and colorectal cancer: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2009; 7(6):676-681.
11. Kaminski MF, Regula J, Kraszewska E, et al. Quality indicators for colonoscopy and the risk of interval cancer. *N Engl J Med*. 2010;362(19):1795-1803.
12. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med*. 2000;343 (3):169-174.
13. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer: Veterans Affairs Cooperative Study Group 380. *N Engl J Med*. 2000;343(3):162-168.
14. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Using risk for advanced proximal colonic neoplasia to tailor endoscopic screening for colorectal cancer. *Ann Intern Med*. 2003;139 (12):959-965.
15. Schoenfeld P, Cash B, Flood A, et al; CONCeRN Study Investigators. Colonoscopic screening of average-risk women for colorectal neoplasia. *N Engl J Med*. 2005;352(20):2061-2068.
16. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Results of screening colonoscopy among persons 40 to 49 years of age. *N Engl J Med*. 2002;346(23):1781-1785.
17. Vogelstein B, Fearon ER, Hamilton SR, et al. Genetic alterations during colorectal-tumor development. *N Engl J Med*. 1988;319(9):525-532.
18. Sung JJY, Lau JYW, Young GP, et al; Asia Pacific Working Group on Colorectal Cancer. Asia Pacific consensus recommendations for colorectal cancer screening. *Gut*. 2008;57(8):1166-1176.
19. Malignant neoplasias of colon over time [in German]. Statistics Austria. http://www.statistik.at/web_de/statistiken/gesundheit/krebserkrankungen/dickdarm_enddarm/020512.html. Accessed September 1, 2011.
20. Atkin WS, Edwards R, Kralj-Hans I, et al; UK Flexible Sigmoidoscopy Trial Investigators. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet*. 2010;375(9726):1624-1633.
21. Hoffmeister M, Schmitz S, Karmrodt E, et al. Male sex and smoking have a larger impact on the prevalence of colorectal neoplasia than family history of colorectal cancer. *Clin Gastroenterol Hepatol*. 2010; 8(10):870-876.
22. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM; American College of Gastroenterology. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [published correction in *Am J Gastroenterol*. 2009;104(6):1613]. *Am J Gastroenterol*. 2009; 104(3):739-750.
23. Lieberman DA, Holub JL, Moravec MD, Eisen GM, Peters D, Morris CD. Prevalence of colon polyps detected by colonoscopy screening in asymptomatic black and white patients. *JAMA*. 2008;300(12):1417-1422.

 ©2011 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013