Neoplasia Yield and Colonoscopic Workload of Surveillance Regimes for Colorectal Cancer in Colitis Patients: A Retrospective Study Comparing the Performance of the Updated AGA and BSG Guidelines

Erik Mooiweer, MD, Andrea E. van der Meulen, MD, PhD,† Adriaan A. van Bodegraven, MD, PhD,‡ Jeroen M. Jansen, MD, PhD,§ Nofel Mahmmod, MD,‖ Joyce Nijsten, MD,* Martijn G. H. van Oijen, MD, PhD,* Peter D. Siersema, MD, PhD,* and Bas Oldenburg, MD, PhD**

Background: Due to the increased risk of colorectal cancer, colonoscopic surveillance is recommended for patients with ulcerative and Crohn's colitis. Because surveillance intervals differ considerably between the recently updated American Gastroenterological Association (AGA) and British Society of Gastroenterology (BSG) guidelines, we compared the neoplasia yield and colonoscopic workload of these guidelines.

Methods: Patients with inflammatory bowel disease undergoing surveillance were identified using medical records. Patients were stratified according to the BSG and AGA guidelines, and corresponding colonoscopic workload was calculated based on the risk factors present during follow-up. The incidence of colitis-associated neoplasia (CAN), defined as a low-grade dysplasia in flat mucosa or a non–adenoma-like mass, high-grade dysplasia, or colorectal cancer was compared between the risk groups of either guidelines.

Results: In total, 1018 patients with inflammatory bowel disease who underwent surveillance were identified. Using the AGA surveillance intervals, 64 patients (6%) were assigned to annual and 954 patients (94%) to biannual surveillance, resulting in 541 colonoscopies per year. The yield of CAN was 5.3% and 20.3% in the low- and high-risk groups, respectively ($P = 0.02$). Using the BSG surveillance intervals, 204 patients received surveillance annually (20%), 393 patients every 3 years (39%), and 421 patients every 5 years (41%), resulting in 420 colonoscopies per year, which is 22% lower than the AGA guidelines. The yield of CAN was 3.6%, 6.9%, and 10.8%, for the low-, intermediate-, and high-risk groups, respectively ($P = 0.26$).

Conclusions: Although the BSG surveillance intervals offer the advantage of a lower colonoscopic workload, the risk stratification of the AGA seems superior in distinguishing patients at higher risk of CAN.

(Inflamm Bowel Dis 2013;19:2603–2610)

Key Words: inflammatory bowel disease, colorectal cancer, surveillance, guidelines

Patients with longstanding extensive ulcerative colitis (UC) and Crohn's colitis are at an increased risk of developing colorectal cancer (CRC).[1] For this reason, colonoscopic surveillance has been advocated, although solid evidence that this indeed prolongs survival is lacking.[2] In 2002, both the American Gastroenterological Association (AGA) and the British Society of Gastroenterology (BSG) published their first guidelines describing which patients should undergo surveillance and how this should be performed.[3,4] Although there were some differences regarding the recommended surveillance intervals between these guidelines, both stated that regular surveillance with an interval between 1 and 3 years should be performed after 8 to 10 years of disease duration in case of at least extensive colitis and after 15 to 20 years in patients with left-sided disease. Because CRC risk in UC and Crohn's colitis seems to be similar for comparable extent and duration, these guidelines are considered to be applicable to patients with Crohn's colitis as well.[5]

Both the BSG and the AGA guidelines were recently updated to implement new endoscopic techniques and improved risk stratification.[6,7] Although both guidelines still recommend regular surveillance in all patients with extensive colitis and now endorse the use of chromoendoscopy, there is no consensus regarding the intervals between surveillance colonoscopies. The new BSG guidelines adopt an algorithm based on established risk factors for colitis-associated CRC to stratify patients in a high-, intermediate-, and low-risk group with adjusted surveillance intervals. The most striking difference as compared with the previous

Received for publication July 19, 2013; Accepted July 29, 2013.

From the *Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, the Netherlands; †Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the Netherlands; ‡Department of Gastroenterology and Hepatology, VU Medical Center Amsterdam, Amsterdam, the Netherlands; §Department of Gastroenterology and Hepatology, OLVG Amsterdam, Amsterdam, the Netherlands; and ‖Department of Gastroenterology and Hepatology, St Antonius Hospital Nieuwegein, Nieuwegein, the Netherlands.

The authors have no conflicts of interest to disclose.

Reprints: Bas Oldenburg, MD, PhD, Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands (e-mail: b.oldenburg@umcutrecht.nl).

DOI 10.1097/MIB.0b013e3182a74b27

Published online 11 September 2013.

BSG guidelines is that the low-risk group is now recommended to undergo surveillance every 5 years. The same risk factors are mentioned in the updated AGA guidelines, but the authors state that optimal surveillance intervals cannot be clearly defined and therefore recommend surveillance every 1 to 3 years.

Although longer surveillance intervals offer an advantage in terms of colonoscopic workload and cost reduction, the drawback could be a higher number of interval cancers, thereby reducing its effectiveness. Because a head-to-head comparison of the updated BSG and AGA guidelines will probably never be performed, we aimed to establish the guidelines that can identify patients at risk for neoplasia best. Furthermore, we assessed differences in colonoscopic workload between the new AGA and BSG guidelines.

METHODS

Patients

All patients with a diagnosis of Crohn's disease (CD) or UC from 3 university hospitals and 2 general hospitals were identified using the Diagnosis Treatment Combinations (DTCs) for inflammatory bowel disease (IBD). DTCs are based on the *International Classification of Disease, Ninth Revision*, and can be considered the Dutch version of the Diagnosis Related Groups that are used in other countries, for example, the United States.[8]

The medical records and endoscopy reports of all patients with a DTC code for CD or UC were reviewed to confirm the IBD diagnosis and to assess whether patients had a valid indication for surveillance colonoscopy according to the new AGA and BSG guidelines. Because the new BSG and AGA guidelines do not concur with regard to the beginning of surveillance (10 and 8 years after the onset of colitis symptoms, respectively), we considered patients with a disease duration of at least 8 years eligible for surveillance. Patients with colitis and a concomitant diagnosis of primary sclerosing cholangitis (PSC) were considered to have an indication for surveillance immediately after diagnosis, whereas patients with proctitis or proctosigmoiditis (patients with UC) or with involvement of $<30\%$ of the colonic mucosa in case of CD were considered to have no indication for surveillance and were excluded.

During the study period, all participating centers performed surveillance in accordance with international guidelines, i.e., complete colonic inspection including biopsy sampling of all areas suspicious for neoplasia with or without the use of chromoendoscopy and sampling of 4 random biopsies every 10 cm when chromoendoscopy was not performed. Standard bowel preparation consisted of 4 L of polyethylene glycol solution.

All endoscopy reports were reviewed to confirm that patients underwent at least 1 surveillance colonoscopy. A surveillance colonoscopy was defined as a procedure with the clear intention to detect neoplasia (explicitly stated as the indication for the colonoscopy and/or by taking 4 quadrant random biopsies every 10 cm). Exclusion criteria were any previous diagnosis of neoplasia (other than discrete solitary sessile or pedunculated polyps resembling sporadic adenomas and containing adenomatous tissue on histology) or (sub)total colectomy before the first surveillance colonoscopy.

Data Collection

Demographic and clinical data were collected from the medical records and included date of IBD diagnosis, type of IBD, disease extent before the start of surveillance, family history of CRC, medication use, and a concomitant diagnosis of PSC. Disease extent before the first surveillance colonoscopy was defined as the maximum extent according to either the histology or endoscopy reports. In UC and IBD-unclassified, disease extent was defined as either left-sided or extensive (inflammation distal or proximal to the splenic flexure, respectively). In patients with Crohn's colitis, involvement of ≥ 3 anatomical parts of the colon was considered extensive disease, whereas involvement of 1 or 2 sections was considered limited diseases.

Neoplasia

For all suspected dysplastic lesions, the location and endoscopic description was recorded. Based on the pathology report, lesions were categorized as nondysplastic, indefinite for dysplasia, low-grade dysplasia (LGD), high-grade dysplasia (HGD), or CRC. Endoscopically visible lesions containing LGD were subdivided in adenoma-like mass (discrete solitary sessile or pedunculated polyps resembling sporadic adenomas and containing adenomatous tissue on histology) and non–adenoma-like mass (all other endoscopic descriptions, i.e., plaque-like lesions, irregular masses). Our primary endpoint was colitis-associated neoplasia (CAN), defined as patients developing a non–adenoma-like mass containing LGD, flat dysplasia (LGD or HGD), HGD, or CRC.

Follow-up

Patients were followed up from the date of the first surveillance colonoscopy until one of the following endpoints: (1) last surveillance colonoscopy, (2) (sub)total colectomy, (3) death, and (4) diagnosis of CAN.

Endoscopic risk factors were scored at each surveillance colonoscopy during follow-up including extent and severity of inflammation, presence of postinflammatory polyps, and strictures. Severity of endoscopic and histologic inflammation was scored as no, mild, moderate, or severe inflammation as specified in the endoscopy and histology report. Patients were scored as positive for each risk factor when this was present at one or more surveillance colonoscopies during follow-up.

Surveillance Intervals

The enrolled patients were stratified in the risk groups as specified in the new AGA and BSG guidelines to calculate the colonoscopic workload of surveillance and to compare the yield of CAN between the risk groups. Details about the risk factors used by either guideline are provided in Figure 3.

Statistical Analysis

Baseline patient and endoscopic characteristics during the surveillance colonoscopies were analyzed using standard descriptive statistics. The cumulative incidence of CAN was calculated for the different risk strata according to the BSG and AGA guidelines using Kaplan–Meier analysis and comparisons between risk groups were made with log-rank testing. Patients who did not develop CAN were censored at the moment of last surveillance colonoscopy or colectomy. To test the discriminative power of the risk groups of either guideline in identifying patients with CAN, the C-statistic was calculated using Cox regression analysis.

To calculate the colonoscopic workload of the BSG and AGA guidelines, the contribution of each patient to the average annual number of surveillance colonoscopies was calculated based on the intervals described in either guideline. Univariate and multivariate analysis was performed using Cox regression analysis to identify predictors for the development of CAN. A 2-sided P value <0.05 was considered statistically significant. Data were analyzed using SPSS version 2.0 for Windows.

Ethical Considerations

This study was carried out with the approval of and in accordance with the ethical guidelines of the medical ethical committee of our institution.

RESULTS

Patients

Our search identified 4514 patients with a DTC code for CD or UC. Surveillance was performed in 1018 patients (23%), of whom 408 had Crohn's colitis (40%), 573 had UC (56%), and 37 had indeterminate colitis (4%). Baseline characteristics of the study population are shown in Table 1.

TABLE 1. Baseline Characteristics of Patients Undergoing Surveillance

	N (%)
No. of patients	1018 (100)
Male sex	491 (48)
Type of hospital	
Referral center	737 (73)
General hospital	281 (27)
IBD diagnosis	
UC	573 (56)
Distal splenic flexure	252 (44)
Proximal splenic flexure	309 (54)
Unknown	12 (2)
Crohn's colitis	408 (40)
Segmental colitis <50%	173 (42)
Segmental colitis >50%	216 (53)
Unknown	19 (5)
Indeterminate colitis	37 (4)
Segmental colitis <50%	17 (46)
Segmental colitis >50%	19 (51)
Unknown	1 (3)
Age at first surveillance colonoscopy, yr (mean ± SD)	46.7 (±12.6)
Duration of IBD at first surveillance colonoscopy, yr (mean ± SD)	16.7 (±8.3)
Concomitant diagnosis of PSC	64 (6)
Medication use (>3 mo)	
5-ASA	880 (86)
AZA	480 (47)
Methotrexate	75 (7)
Biologics	165 (16)
Duration of follow-up, yr (median, range)	2.6 (0–12.5)
Partial or total colonic resection during follow-up	78 (8)

Surveillance Colonoscopies

In total, 2371 surveillance colonoscopies were performed during the follow-up, with a median of 2 surveillance colonoscopies per patient (range, 1–10). Bowel preparation was judged to be adequate in 90% of surveillance colonoscopies, and the cecal intubation rate was 97%. Chromoendoscopy was used in 53 surveillance colonoscopies (2%), whereas random biopsies were taken in the remaining 2318 colonoscopies (98%).

Active endoscopic inflammation was present in 777 (33%) of surveillance colonoscopies and active histologic inflammation in 947 (40%) surveillance colonoscopies (Table 2). Postinflammatory polyps were encountered in 506 surveillance colonoscopies in 257 patients (25%).

Neoplasia During Follow-up

Neoplasia was detected during 1 or more of the follow-up surveillance colonoscopies in 173 patients (15%) (Table 3). Based on the endoscopy and histopathology reports, 64 (5%) patients developed CAN during follow-up: 11 patients developed CRC, 6 patients HGD, 32 patients flat LGD and 15 patients a non–adenoma-like mass with LGD (Table 3). The remaining 109 patients developed either indefinite for dysplasia (11 patients) or an adenoma-like mass containing LGD (98 patients). The cumulative incidence of CAN by disease duration was 0.9% at 10 years, 6.2% at 20 years, 16.9% at 30 years, and 35.3% at 40 years (Fig. 1).

Low-grade Dysplasia

Flat LGD was diagnosed in 36 patients, of whom 2 patients progressed to HGD and 2 to CRC (Fig. 2). Flat LGD was unifocal in 26 patients (72%) and located distally to the splenic flexure in 19 patients (53%).

A non–adenoma-like mass containing LGD was found in 16 patients (9 proximal to the splenic flexure, median size 16 mm [range, 2–30]), which was treated by colectomy in 6 patients. In none of these cases, HGD or CRC was detected in the colectomy specimen. In 10 patients, the lesion was treated endoscopically. In

TABLE 2. Endoscopic Characteristics

	N (%)
No. of colonoscopies	2371 (100)
Cecal intubation	2301 (97)
Suboptimal bowel preparation	244 (10)
No. of biopsies per colonoscopy (mean ± SD)	
Random biopsy protocol	27 (±10)
Chromoendoscopy protocol	9 (±5)
Endoscopic inflammation	
No signs of previous or present inflammation	266 (11)
Quiescent disease	1328 (56)
Mild	621 (26)
Moderate to severe	156 (7)
Histologic inflammation	
No signs of previous or present inflammation	110 (5)
Quiescent disease	1314 (55)
Mild	790 (33)
Moderate or severe	157 (7)
Postinflammatory polyps	506 (21)
Stricture	
UC	10 (1)
Crohn's colitis	65 (3)

one of these patients, who was operated on for refractory disease 3 years after removal of the non–adenoma-like mass, CRC was unexpectedly diagnosed in the ileocecal resection specimen.

High-grade Dysplasia

HGD was diagnosed in 6 patients during the follow-up (Fig. 2). Two patients developed HGD in an adenoma-like mass, which was treated endoscopically in 1 patient and by colectomy in the other patient. One patient developed flat HGD 1 year after diagnosis of flat LGD, which was not treated by colectomy due to advanced age. Two patients with HGD in a non–adenoma-like mass were found to have synchronous multifocal flat LGD in other segments of the colon. Both were treated by colectomy, which confirmed the diagnoses of LGD and HGD, but revealed no additional advanced neoplasia.

In 1 patient, HGD was diagnosed in biopsies surrounding a non–adenoma-like mass containing LGD. The colectomy specimen confirmed the presence of HGD and LGD with no additional diagnosis of CRC.

TABLE 3. Neoplasia During Follow-up, Based on the Maximal Grade of Dysplasia

	Random Biopsy Protocol (n = 965)	Chromoendoscopy Protocol (n = 53)
Patients diagnosed with neoplasia, n (%)	162 (17)	11 (21)
Indefinite for dysplasia, n (%)	11 (1)	0 (0)
LGD, n (%)		
Adenoma-like mass	89 (9)	9 (17)
Flat dysplasia	31 (3)	2 (4)
Non–adenoma-like mass	15 (1)	0 (0)
HGD, n (%)	6 (0.6)	0 (0)
CRC, n (%)	11 (1)	0 (0)
Dukes A	1	—
Dukes B	5	—
Dukes C	3	—
Dukes D	2	—

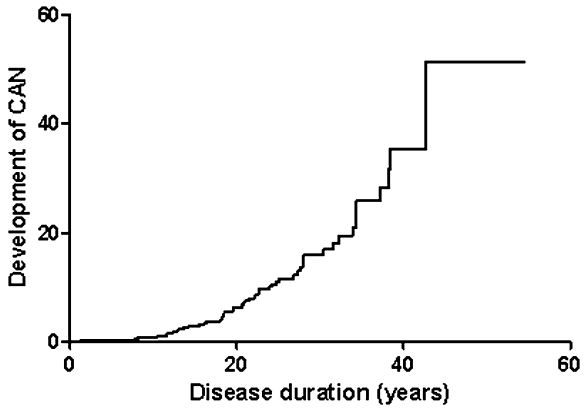

FIGURE 1. Kaplan–Meier curve showing the development of CAN by disease duration. Vertical lines represent events of CAN defined as non–adenoma-like LGD, HGD, or CRC.

Colorectal Cancer

A total of 12 CRC's were diagnosed in 11 patients during follow-up at a median age of 59 years (range, 39–69) (Fig. 2). In 5 patients, CRC was diagnosed without a previous diagnosis of neoplasia, despite the fact that all patients underwent at least 1 surveillance colonoscopy before the CRC diagnosis with a median interval between the last surveillance colonoscopy and the CRC diagnosis of 26 (range, 20–47) months.

In 6 patients, dysplasia was detected during surveillance colonoscopies before the diagnosis of CRC. The dysplasia diagnosis was flat indefinite for dysplasia in 2 patients and LGD in 4 patients (Fig. 2).

Surveillance Intervals According to the New BSG Guidelines

Based on risk factors present during follow-up, surveillance intervals were determined according to the AGA and BSG guidelines in all 1018 patients. When applying the new BSG guidelines, 421 patients (41%) were assigned to the low-risk group (surveillance interval of 5 yr), 393 patients (39%) to the intermediate-risk group (surveillance interval of 3 yr), and 204 patients (20%) to the high-risk group (annual surveillance interval) (Fig. 3). CAN was detected in 15 low-risk patients

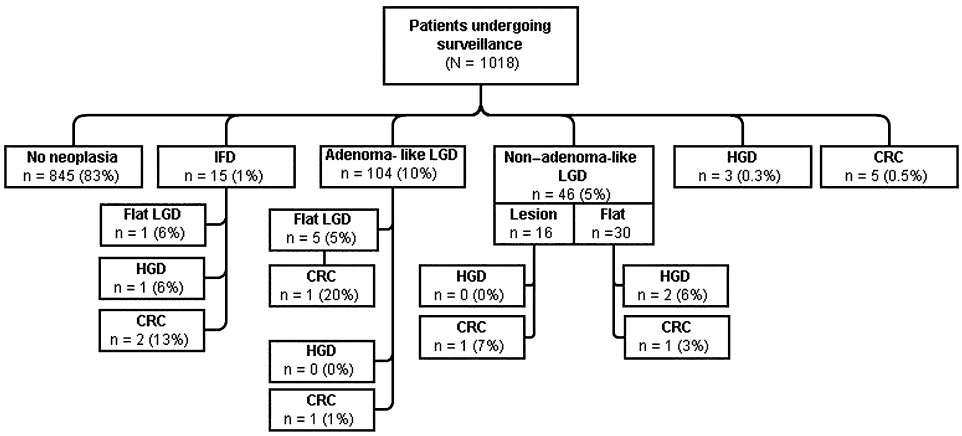

FIGURE 2. Flow chart showing the development of neoplasia during follow-up.

(3.6%; 14 LGD, 0 HGD, and 1 CRC), in 27 intermediate-risk patients (6.9%; 21 LGD, 0 HGD, and 6 CRC), and in 22 high-risk patients (10.8%; 12 LGD, 6 HGD, and 4 CRC). The 5-year cumulative incidence of CAN was 5.6%, 7.2%, and 9.9% for the low-, intermediate-, and high-risk groups, respectively (Fig. 4) (low versus high risk $P = 0.07$, low versus medium $P = 0.48$, and medium versus high $P = 0.33$; log-rank test). If the primary endpoint was limited to cases of HGD or CRC, the 5-year cumulative incidence was 0.7%, 1.8%, and 4.3% for the low-, intermediate-, and high-risk groups, respectively (Fig. 5) (low versus high risk $P < 0.01$, low versus medium $P = 0.21$, medium versus high $P = 0.09$; log-rank test). Using the new BSG intervals resulted in an average annual workload of 420 surveillance colonoscopies, or 0.41 colonoscopies per patient per year. When the 3 risk groups were entered in a Cox regression analysis, the corresponding C-statistic was 0.55.

Surveillance Intervals According to the New AGA Guidelines

In accordance with the new AGA guidelines, 954 patients (94%) were assigned to the low-risk group and 64 patients (6%) to the high-risk group (Fig. 3). CAN was detected in 51 low-risk patients (5.3; 39 LGD, 2 HGD, and 10 CRC) and in 13 high-risk patients (20.3%; 8 LGD, 4 HGD, and 1 CRC). The 5-year cumulative incidence of CAN was 6.3% in the low-risk group and 18.7% in the high-risk group ($P = 0.02$, log-rank) (Fig. 4). If the primary endpoint was limited to cases of HGD or CRC, the

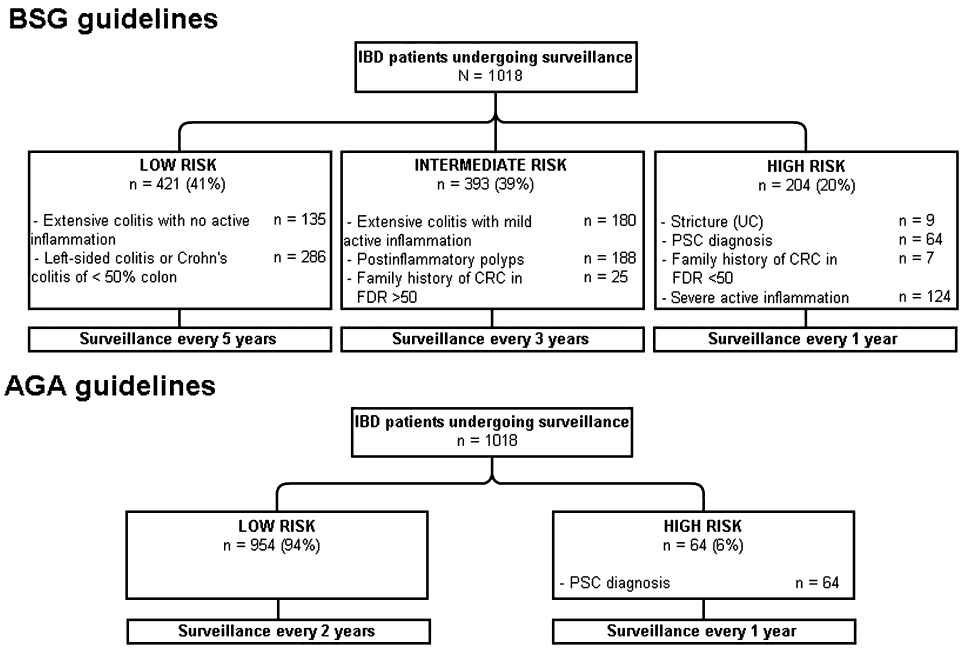

FIGURE 3. Flow chart showing the stratification of patients undergoing surveillance according to the AGA and BSG guidelines. FDR, first-degree relative.

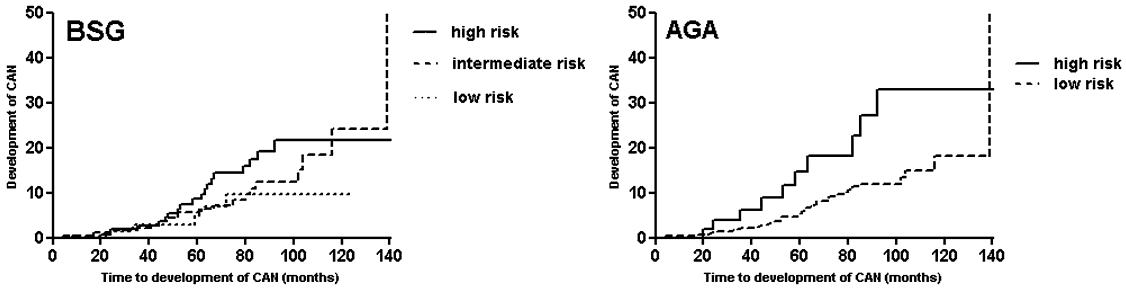

FIGURE 4. Kaplan–Meier curve comparing the cumulative incidence of CAN between the risk groups of the BSG guideline (left) and the AGA guideline (right). CAN is defined as non–adenoma-like LGD, HGD or CRC. Low risk versus high risk, $P = 0.07$; Low versus intermediate, $P = 0.48$; intermediate versus high, $P = 0.33$ (BSG guideline). Low risk versus high risk, $P = 0.02$ (AGA guideline).

5-year cumulative incidence was 1.7% in the low-risk group and 7.2% in the high-risk group ($P = 0.02$, log-rank) (Fig. 5).

The average annual number of surveillance colonoscopies when applying the AGA intervals was 541, or 0.53 per patient per year, when a surveillance interval once every 2 years was used for the low-risk group. When a surveillance interval of 3 years was used for the low-risk group, the average annual number of surveillance colonoscopies drops to 382 or 0.38 per patient per year. Therefore, the colonoscopic workload when adopting the BSG guidelines is 22% less than the workload associated with the AGA guidelines if a surveillance interval once every 2 years for the low-risk group is used. When the 2 risk groups were entered in a Cox proportional hazards model, the corresponding C-statistic was 0.57.

Factors Associated with the Development of CAN

Univariate analysis showed that the development of CAN was significantly associated with male sex (odds ratio [OR], 1.7), a positive family history of CRC (OR, 3.2), PSC (OR, 2.6), the presence of strictures in patients with UC (OR, 4.5), and the absence of histologic inflammation (OR, 0.6). After multivariate analysis the factors PSC, family history of CRC, the absence of histological inflammation and the presence of strictures in patients with UC remained significantly associated with the development of CAN (Table 4).

DISCUSSION

The aim of this retrospective study was to assess whether the risk-stratified approaches of the updated AGA or BSG guidelines for surveillance were more effective in terms of colonoscopic workload and neoplasia yield. The new BSG guidelines were found to only moderately discriminate between the 3 risk groups with regard to the overall incidence of CAN (3.6%, 6.9%, and 10.8% for the low-, intermediate-, and high-risk groups, respectively). In contrast, the overall yield of CAN in the low-risk group of the AGA guidelines was 5.3%, which was significantly lower than the 20.3% for the high-risk group. However, if you compare the predictive power of the risk groups of either guideline using the C-statistic, both guidelines show a similar poor discriminative power with values of 0.55 (BSG) and 0.57 (AGA).

The differences in neoplasia yield come with a cost; however, the risk of CAN in the low-risk group of the AGA guidelines is higher than in the low-risk group of the BSG guidelines (5.3% versus 3.6%). Whether the shorter surveillance intervals of the AGA guideline protect these low-risk patients from developing advanced neoplasia remains to be studied.

A potential advantage of risk stratification is the avoidance of unnecessary colonoscopies. We found that implementation of the BSG guidelines reduced the colonoscopic workload by 22% as compared with the AGA guidelines. The authors of the new BSG guidelines estimated the percentages of patients in each risk

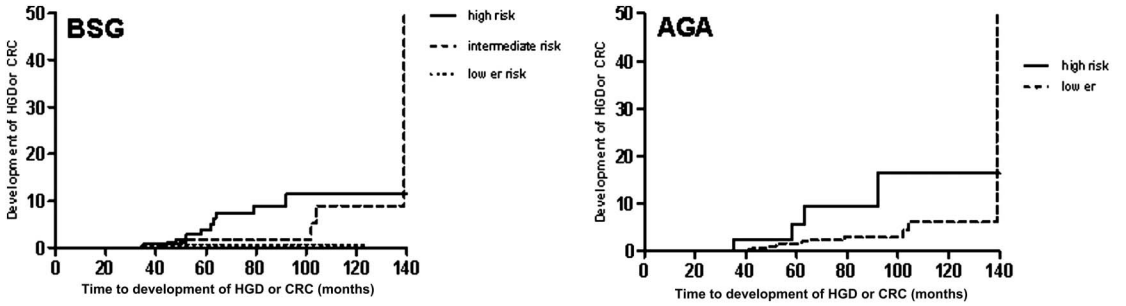

FIGURE 5. Kaplan–Meier curve comparing the cumulative incidence of HGD or CRC between the risk groups of the BSG guideline (left) and the AGA guideline (right). Low-risk versus high-risk, $P < 0.01$; low versus intermediate, $P = 0.21$; intermediate versus high, $P = 0.09$ (BSG guideline). Low risk versus high risk, $P = 0.02$ (AGA guideline).

TABLE 4. Cox Proportional Hazard Analysis of the Association Between Several Known Risk Factors and the Incidence of CAN

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Male sex	1.7 (1.0–2.9)	1.4 (0.80–2.5)
UC (versus CD)	1.3 (0.8–2.2)	1.1 (0.6–2.1)
Extensive colitis	1.0 (0.6–1.8)	0.9 (0.5–1.9)
Endoscopic inflammation		
No inflammation	0.8 (0.5–1.3)	0.8 (0.5–1.5)
Mild	0.7 (0.4–1.1)	0.6 (0.3–1.1)
Moderate/severe	1.2 (0.6–2.3)	0.9 (0.4–2.1)
Histologic inflammation		
No inflammation	0.6 (0.3–1.0)	**0.4 (0.2–0.8)**
Mild	0.8 (0.5–1.3)	0.6 (0.3–1.1)
Moderate/severe	1.2 (0.6–2.1)	1.1 (0.5–2.4)
Stricture (patients with UC)	**4.5 (1.4–14.4)**	**3.8 (1.1–13.3)**
First-degree relative with CRC diagnosis	**3.2 (1.4–7.6)**	**3.9 (1.6–9.5)**
Postinflammatory polyps	1.1 (0.7–1.9)	1.1 (0.6–2.1)
History of PSC	**2.6 (1.4–4.7)**	**2.5 (1.2–5.0)**

group to be 15%, 30%, and 55% for the high-, intermediate-, and low-risk groups, which is more or less in line with our results (20%, 39%, and 41%, respectively).[7] One other study also reported that the colonoscopic workload could be reduced by 15% using the new BSG guidelines.[9]

However, these differences in colonoscopic workload critically depend on arbitrarily chosen surveillance intervals. For example, if a surveillance interval of 3 years would be applied to the lower risk group of the AGA guidelines, the colonoscopic workload would be 9% lower than the workload associated with the BSG guidelines. Because no prospective data are available comparing different surveillance intervals in colitis patients, stratification as defined by the AGA guidelines with a surveillance interval of 3 years for the low-risk group might offer the best compromise with regard to the identification of CAN and the reduction of colonoscopic workload.

Some established risk factors for colitis-associated CRC implemented in the new AGA and BSG guidelines were confirmed in our study. We found a 2.5-fold higher risk of developing CAN in patients with a concomitant diagnosis of PSC, which is in line with earlier reports.[10,11] Patients with a first-degree relative diagnosed with CRC had a higher risk as well, although conflicting data in literature exist on this issue.[12–15] We also confirmed that the absence of histologic signs of inflammation is associated with a reduced risk of developing CRC.[16] Several studies have suggested that endoscopic features reflecting long-standing severe inflammation such as postinflammatory polyps, strictures, and active inflammation during surveillance can predict the risk of subsequent development of neoplasia as well.[14,17] Apart from the association between strictures in patients with UC and neoplasia development, we could not confirm this. Strictures in patients with UC are rare, but if present carry a high risk of CRC.[18,19] In our study, 9 patients with UC developed a stricture, of which 2 developed CRC and 1 HGD, underscoring the need for close surveillance or even colectomy in these patients. The moderate performance of the BSG guidelines in identifying patients at higher risk of CAN in our study can partially be attributed to its strong dependence on endoscopic parameters. Based on our results, it seems questionable whether these factors should be used to stratify patients for surveillance. Our study has several limitations. Due to the retrospective design, patients in this study were not screened in accordance with the updated intervals of the BSG and AGA guidelines, and therefore the longer intervals of 3 and 5 years were not yet implemented. Although the incidence of CAN was used as an endpoint to compare the different risk strata, the potential drawbacks of a longer surveillance interval such as the occurrence of more advanced neoplasia and interval carcinomas could not be assessed. Furthermore, the presence of known risk factors for IBD-associated CRC such as a diagnosis of PSC or the presence of postinflammatory polyps could have triggered an increased awareness from the endoscopists, which could have overestimated the incidence of CAN in these high-risk patients. However, because we found only a moderate discriminative power for the risk factors used in both guidelines, the presence of this bias would only underscore our results.

Despite the fact that more than 1000 patients were included, only 11 patients developed CRC (during 3172 patient-years of follow-up). For that reason, we also included colitis-associated LGD and HGD in a composite endpoint. Especially for lesions with LGD, there is no consensus on how colitis-associated lesions can be distinguished from sporadic adenomas, which could have introduced bias. Furthermore, there is considerable interobserver variability among pathologists for the diagnosis of LGD in the setting of colitis, which could have introduced bias as well because the pathology slides were not reviewed by an expert panel.[20] We aimed to minimize the interference of sporadic adenomas and carcinomas by reviewing the endoscopic and histologic description of each lesion containing dysplasia and excluding all discrete sessile or pedunculated lesions containing adenomatous tissue.

Both the updated AGA and BSG guidelines advocate the use of chromoendoscopy with targeted biopsies because of a superior neoplasia yield over random biopsies.[21] Because most colonoscopies in this study were performed before the publication of these updated guidelines, only 53 colonoscopies (2%) were performed using chromoendoscopy. Whether chromoendoscopy performs better among high-risk patients as compared with the intermediate- or low-risk patients is currently unknown, and therefore we refrain from speculation how chromoendoscopy would have affected the results if used in the majority of patients. Patients were stratified for their next surveillance interval, but we were unable to incorporate changing surveillance intervals during follow-up due to transient risk factors, particularly

inflammation. We believe, however, that although some patients will be assigned to other surveillance intervals because of this, the total number of patients with active inflammation will remain approximately stable over time, and therefore the influence on colonoscopic workload is probably small.

Due to the retrospective design, we relied on the endoscopy reports to determine whether endoscopic risk factors such as active inflammation or postinflammatory polyps were present. The fact that endoscopists might interpret the endoscopic findings differently could have resulted in an overestimation or underestimation of the presence of these factors. Furthermore, well-defined and validated endoscopic and histologic scores reliably reflecting the severity of inflammation were not used.

We included both patients with UC and Crohn's colitis in this study. Although several studies indicate that the risk of CRC is similar when disease extent and duration are comparable, most studies reporting on risk factors for developing CRC only include patients with UC.[14,17,22] It might well be that risk factors for CRC are different in patients with Crohn's colitis, which could have affected our results. However, in the univariate and multivariate analysis of individual risk factors, the type of IBD was not associated with the development of CAN.

In conclusion, this study shows the clinical consequences if the new AGA or BSG guidelines are applied to a large cohort of patients with IBD undergoing surveillance. Although the longer surveillance intervals of the new BSG guidelines reduce the colonoscopic workload considerably compared with the AGA guidelines, the risk strata as defined in the AGA guidelines are superior in distinguishing patients at high and low risk of CAN. Furthermore, if a 3-year surveillance interval is applied to the lower risk group of the AGA guidelines, the workload is 9% lower compared with the BSG guidelines. Whether the lower incidence of CAN in the low-risk groups of both guidelines justifies longer surveillance intervals is presently unknown and should be the focus of future studies.

REFERENCES

1. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut*. 2001;48:526–535.
2. Mpofu C, Watson AJ, Rhodes JM. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. *Cochrane Database Syst Rev.* 2004;CD000279.
3. Cairns S, Scholefield JH. Guidelines for colorectal cancer screening in high risk groups. *Gut*. 2002;51(suppl 5):V1–V2.
4. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. *Gastroenterology*. 2003;124:544–560.
5. Gillen CD, Walmsley RS, Prior P, et al. Ulcerative colitis and Crohn's disease: a comparison of the colorectal cancer risk in extensive colitis. *Gut*. 1994;35:1590–1592.
6. Farraye FA, Odze RD, Eaden J, et al. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. *Gastroenterology*. 2010;138:738–745.
7. Cairns SR, Scholefield JH, Steele RJ, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). *Gut*. 2010;59:666–689.
8. Enthoven AC, van de Ven WP. Going Dutch—managed-competition health insurance in the Netherlands. *N Engl J Med.* 2007;357:2421–2423.
9. Elsadani NN, East JE, Walters JR. New 2010 British Society of Gastroenterology colitis surveillance guidelines: costs and surveillance intervals. *Gut*. 2011;60:282–283.
10. Claessen MM, Vleggaar FP, Tytgat KM, et al. High lifetime risk of cancer in primary sclerosing cholangitis. *J Hepatol.* 2009;50:158–164.
11. Soetikno RM, Lin OS, Heidenreich PA, et al. Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. *Gastrointest Endosc.* 2002;56:48–54.
12. Askling J, Dickman PW, Karlen P, et al. Colorectal cancer rates among first-degree relatives of patients with inflammatory bowel disease: a population-based cohort study. *Lancet.* 2001;357:262–266.
13. Nuako KW, Ahlquist DA, Mahoney DW, et al. Familial predisposition for colorectal cancer in chronic ulcerative colitis: a case-control study. *Gastroenterology*. 1998;115:1079–1083.
14. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. *Gastroenterology*. 2004;126:451–459.
15. Jess T, Loftus EV Jr, Velayos FS, et al. Risk factors for colorectal neoplasia in inflammatory bowel disease: a nested case-control study from Copenhagen county, Denmark and Olmsted county, Minnesota. *Am J Gastroenterol.* 2007;102:829–836.
16. Gupta RB, Harpaz N, Itzkowitz S, et al. Histological inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: a cohort study. *Gastroenterology*. 2007;133:1099–1105.
17. Rutter MD, Saunders BP, Wilkinson KH, et al. Cancer surveillance in longstanding ulcerative colitis: endoscopic appearances help predict cancer risk. *Gut*. 2004;53:1813–1816.
18. Gumaste V, Sachar DB, Greenstein AJ. Benign and malignant colorectal strictures in ulcerative colitis. *Gut*. 1992;33:938–941.
19. Reiser JR, Waye JD, Janowitz HD, et al. Adenocarcinoma in strictures of ulcerative colitis without antecedent dysplasia by colonoscopy. *Am J Gastroenterol.* 1994;89:119–122.
20. van Schaik FD, ten Kate FJ, Offerhaus GJ, et al. Misclassification of dysplasia in patients with inflammatory bowel disease: consequences for progression rates to advanced neoplasia. *Inflamm Bowel Dis.* 2011;17:1108–1116.
21. Rutter MD, Saunders BP, Schofield G, et al. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. *Gut*. 2004;53:256–260.
22. Velayos FS, Loftus EV Jr, Jess T, et al. Predictive and protective factors associated with colorectal cancer in ulcerative colitis: a case-control study. *Gastroenterology*. 2006;130:1941–1949.