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Using New Hampshire Colonoscopy Registry data to assess United States and European post-polypectomy surveillance guidelines

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Abstract

Background—Our goal was to compare the updated European Society of Gastrointestinal Endoscopy (ESGE) and United States Multi-Society Task Force on Colorectal Cancer (USMSTF) high risk groups in predicting metachronous advanced neoplasia on first follow-up colonoscopy and long-term colorectal cancer (CRC).

Methods—We compared advanced metachronous neoplasia risk (serrated polyps ≥ 1 cm or with dysplasia, advanced adenomas ≥ 1 cm, villous, high grade dysplasia), CRC on first surveillance colonoscopy in patients with high risk findings according to ESGE versus USMSTF guidelines. We also compared the positive and negative predictive values (PPV, NPV) of both guidelines for metachronous neoplasia.

Results—The risk for metachronous neoplasia in our sample ($n = 20458$) was higher in the high risk USMSTF (3 year) (13.6 %; 95 % CI 12.3–14.9) and ESGE groups (13.6 %; 95 % CI 12.3–15.0) compared with the lowest risk USMSTF (5.1 %; 95 % CI 4.7–5.5; $P < 0.001$) and ESGE categories (6.3 %; 95 % CI 6.0–6.7; $P < 0.001$), respectively. Adding other groups such as USMSTF 5–10-year and 3–5-year groups to the 3-year category resulted in minimal change in the

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Competing interests

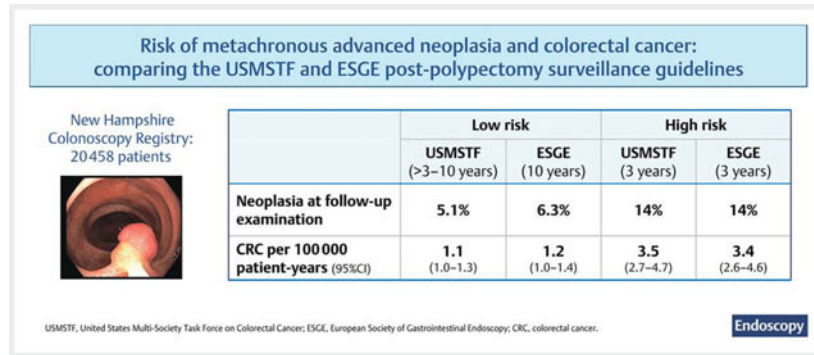
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PPV and NPV for metachronous advanced neoplasia. High risk ESGE (hazard ratio [HR] 3.03, 95 %CI 1.97–4.65) and USMSTF (HR 3.07, 95 %CI 2.03–4.66) designations were associated with similar long-term CRC risk (CRC per 100000 person-years: USMSTF 3-year group 3.54, 95 %CI 2.68–4.68; ESGE high risk group: 3.43, 95 %CI 2.57–4.59).

Conclusion—Performance characteristics for the ESGE and USMSTF recommendations are similar in predicting metachronous advanced neoplasia and long-term CRC. The addition of risk groups, such as the USMSTF 5–10-year and 3–5-year groups to the USMSTF 3-year category did not alter the PPV or NPV significantly.

GRAPHICAL ABSTRACT



Introduction

Surveillance colonoscopy guidelines for adenomas and serrated polyps were updated by the European Society of Gastrointestinal Endoscopy (ESGE) and US Multi-Society Task Force on Colorectal Cancer (USMSTF) in 2020 [1, 2]. Although both guidelines recommend a 3-year surveillance interval for adenomas that are large (≥ 1 cm) or multiple (≥ 5) or have high grade dysplasia (HGD), only the USMSTF considers villous/tubulovillous adenomas, regardless of size, as high risk lesions, requiring a 3-year follow-up. In addition, the USMSTF further stratifies serrated polyps based on their histologic subtypes: hyperplastic polyps (HPPs), sessile serrated polyps (SSPs), and traditional serrated adenomas (TSAs) [1–3].

Whereas the ESGE considers all serrated polyps with dysplasia or that are ≥ 1 cm including HPPs as high risk lesions with a 3-year follow-up recommendation, the USMSTF classifies only SSPs ≥ 1 cm or with dysplasia, 5–10 SSPs < 1 cm, and TSAs as high risk requiring a 3-year follow-up, and recommends a 3–5-year interval for large (≥ 1 cm) HPPs. In addition, the USMSTF has four further risk groups with various recommended intervals for SSPs or tubular adenomas < 1 cm. The ESGE has only two risk groups: a high risk 3-year interval and a low risk group, with recommendation to return to screening after 10 years. Differences in recommendations may be due in part to the weight given to published data. Whereas the ESGE guideline emphasizes data examining risk of colorectal cancer (CRC) incidence and mortality, the USMSTF guideline considers these data as well as data on risk for metachronous advanced polyps [1,2]. There are no published studies comparing the updated USMSTF and ESGE guidelines with respect to ability to predict metachronous risk.

Our objective was to compare the ability of the high risk groups in the USMSTF and ESGE guidelines to identify patients at high risk of future CRC or advanced polyps. We also examined predictive ability of the different risk groups within the USMSTF guideline, with surveillance intervals of 3, 3–5, 5–10, and 7–10 years. Our primary outcome was any metachronous advanced colorectal neoplasia (advanced adenomas, CRC, and large [> 1 cm] or dysplastic serrated polyps). However, as the current USMSTF and ESGE surveillance guidelines provide recommendations for two different pathways to CRC (conventional and serrated), we also separately examined the risk for metachronous advanced adenomas to assess surveillance of index conventional adenomas and the risk for metachronous large (> 1 cm) or dysplastic serrated polyps to assess surveillance of index serrated polyps. We also compared the long-term risk for CRC for those determined to be high risk in the ESGE guidelines and for the various increased-risk categories in the USMSTF recommendations.

Methods

Population

Our cohort included patients in the New Hampshire Colonoscopy Registry (NHCR) database who underwent colonoscopy in 2004–2019 and completed questionnaires before the colonoscopy, which included questions on demographics such as age, sex, and weight, as well as prior history of polyps or CRC and family history. A procedure form, which included colonoscopy information such as polyp findings, was completed during or immediately after colonoscopy by the endoscopist or endoscopy nurse. Pathology reports for each procedure, which included polyp histology, size, and location, were entered by a trained staff member, with pathology information linked to the polyp-level data from the procedure form. Data collection was approved by the Committee for the Protection of Human Subjects at Dartmouth College (CPHS#00015834).

Cohort

We included patients with a polyp found on index examination who underwent surveillance colonoscopy at 12 months after the index examination. We excluded patients with a history of inflammatory bowel disease, polyposis syndromes, CRC, ≥ 10 adenomas, piecemeal resection of ≥ 20 mm polyps, or ≥ 20 serrated polyps on index examinations, and examinations with poor bowel preparation or that were incomplete.

Exposure variables

We assigned each patient an ESGE and a USMSTF risk category as shown in Fig. 1.

- The ESGE categories were high risk (3-year intervals for large [≥ 1 cm] adenomas or those with HGD, large [≥ 1 cm] serrated polyps or those with dysplasia, or 5–10 adenomas) and low risk (all serrated polyps without dysplasia < 1 cm and all tubular adenomas < 1 cm and < 5 in number)
- USMSTF categories were:

- High risk (3-year interval group for large adenomas or those with HGD or villous/tubulovillous histology, all TSAs, SSPs \geq 1 cm or with dysplasia or 5–10 tubular adenomas or SSPs $<$ 1 cm)
- 3–5-year interval group for large (\geq 1 cm) HPPs or 3–4 tubular adenomas or SSPs $<$ 1 cm
- 5–10-year interval group for 1–2 SSPs $<$ 1 cm
- 7–10-year interval group for 1–2 tubular adenomas $<$ 1 cm, and
- 10-year follow-up group for examinations without adenomas and serrated polyps except HPPs $<$ 1 cm.

Outcomes

The primary outcome of interest was the detection of metachronous advanced neoplasia, defined as a combined outcome of large (\geq 1 cm) or dysplastic serrated polyps, advanced adenomas, or CRC on follow-up colonoscopy. Advanced adenomas were defined as any adenoma \geq 1 cm, with villous/tubulovillous histology, or HGD. To assess the impact of the index risk groups on the different pathways, serrated and conventional, we also separately examined the risk for metachronous large (\geq 1 cm) or dysplastic serrated polyps and for advanced adenomas. The primary analysis compared the ESGE high risk category with the USMSTF 3-year category, as well as to their respective low risk groups, but we also examined the other USMSTF increased-risk categories.

We also examined the long-term risk for CRC in all events in the NHCR (i.e. not just each patient's first surveillance colonoscopy after index). We included CRCs from the New Hampshire State Cancer Registry, which is linked to the NHCR.

Statistical analysis

We present the absolute risks for metachronous advanced neoplasia for each USMSTF and ESGE risk category based on results of first follow-up colonoscopy. In addition, we present the incidence per 100 000 person-years for the main outcome. We compared the risk for each of the three outcomes (large [\geq 1 cm] or dysplastic serrated polyps, advanced adenomas, and CRC, as well as the combined outcome) in each of the four high- and increased-risk USMSTF categories with that of the USMSTF 10-year follow-up group (examinations without adenomas and no serrated polyps except HPPs $<$ 1 cm) as a reference. For the ESGE classification, we compared the risk for the three outcomes in the high risk group with that of the low risk group.

We also examined the additional incremental impact of each USMSTF category on the positive predictive value (PPV) and negative predictive value (NPV) for all three outcomes. In other words, we assessed the following USMSTF surveillance interval groups: 3 and 3–5 years combined; 3, 3–5, and 5–10 years combined; and 3, 3–5, 5–10, and 7–10 years combined. PPV was calculated as the number of patients in the high risk category with metachronous neoplasia correctly identified or detected in patients in that risk group (e.g. USMSTF 3-year or USMSTF 3- and 3–5-year groups combined), divided by the total number of patients in that risk group. NPV was calculated as the number of individuals

correctly identified as not at risk for metachronous colorectal neoplasia (e. g. not assigned to the risk group and with no neoplasia found at follow-up colonoscopy) divided by the total number in the low risk group. We also calculated number needed to diagnose by dividing the number of patients in the high risk groups by the number of patients diagnosed with advanced neoplasia in the high risk group.

We used the chi-squared test and Fisher's exact test to compare the risk for each of the three outcomes (large [≥ 1 cm] or dysplastic serrated polyps, advanced adenomas, and CRC, as well as the combined outcome). To assess the association of each set of risk classification categories with metachronous outcomes, we conducted multivariable logistic regressions adjusting for age, sex, body mass index, and months to follow-up. Follow-up time in months in the analysis was the observed interval and not necessarily that dictated by the guidelines. We conducted one regression comparing the ESGE high and low risk groups, and one corresponding to each of the different combinations of USMSTF groups: the 3-year group vs. all other groups; the 3-year and 3–5-year groups combined vs. the other groups; the 3-year, 3–5-year, and 5–10-year groups combined vs. other groups; and finally, the combined 3-year, 3–5-year, 5–10-year, and 7–10-year groups vs. the negative examination (10-year) group.

For the outcome examining long-term risk for CRC, we used all follow-up data for CRC including examinations performed after the first follow-up colonoscopy. Thus, some CRC patients may have had more than one follow-up examination. In addition, in terms of the timing of surveillance examinations included in our analysis, we used a cutoff of 3 months after index colonoscopy as opposed to 12 months used in the other analyses. To assess the association of the long-term hazard of CRC with each set of categories, we used Cox's proportional hazards model adjusting for age, sex, year of examination, bowel preparation, and having more than one surveillance examination after index. For each patient, we calculated follow-up time (months) from the date of their index examination until the time of the second colonoscopy or CRC diagnosis. All *P* values in our analyses were two sided. Analyses were carried out using SPSS Statistics for Macintosh, Version 28.0 (IBM Corp, Armonk, New York, USA).

Results

Our analyzed sample included 20 458 patients in the NHCR who underwent a complete index colonoscopy with adequate bowel preparation and a follow-up examination 12 months after the index examination. The examinations were performed between 2004 and 2019 (index median examination year 2010 [interquartile range (IQR) 6] and surveillance median examination year 2016 [IQR 4]). We stratified according to USMSTF guidelines based on index examination findings: low risk group (no adenomas but HPPs < 1 cm: $n = 11226$), 7–10-year group ($n = 5222$), 5–10-year group ($n = 400$), 3–5-year group ($n = 1093$), and 3-year group ($n = 2517$). We also stratified by the ESGE guidelines: high risk 3-year group ($n = 2450$) vs. low risk group ($n = 18008$). Table 1 details baseline characteristics stratified by both USMSTF and ESGE risk classification.

The metachronous risk for the combined outcome of advanced adenomas, CRC, or large (> 1 cm) or dysplastic serrated polyps was significantly higher in both the USMSTF 3-year group and ESGE high risk categories (13.6 % for USMSTF and 13.6 % for ESGE), compared with the USMSTF low risk group (5.1 %; $P < 0.001$) and the ESGE low risk group (6.3 %; $P < 0.0001$), respectively (Table 2). To make an equal comparison for the ESGE groups, we compared the risk for metachronous advanced neoplasia for the ESGE high risk group (13.6 %) with that of the USMSTF 10-year group (5.1 %) and observed similar results to the comparison between ESGE high and low risk groups ($P < 0.0001$). The absolute risk for advanced adenomas on follow-up was significantly higher in the USMSTF 3-year (9.0 %), 3–5-year (7.6 %), and 7–10-year (5.1 %) groups than for the USMSTF low risk negative examination category (2.8 %), whereas the USMSTF 5–10-year group, at 4.0 %, did not differ significantly from the low risk negative examination category. The absolute risk for future large (> 1 cm) or dysplastic serrated polyps was highest at 10.0 % in the USMSTF 5–10-year category, which includes 1–2 small SSPs, but otherwise ranged from 1.9 % (USMSTF low risk group) to 4.7 % (ESGE high risk) in all other categories.

Combining the USMSTF 3, 3–5, 5–10, and 7–10-year interval groups yielded the highest NPV for metachronous advanced neoplasia, at 94.9 %, but the difference from the USMSTF 3-year group (93.7 %) was minimal. The PPV was highest in the ESGE high risk and USMSTF 3-year categories at 13.6 % (Table 3). The PPV and NPV for each guideline category for metachronous large or dysplastic serrated polyps and advanced adenomas are shown in Table 1 s in the online-only Supplementary material. Results from logistic regression models are shown in Table 3.

To examine the impact of follow-up time on our results, we performed a sensitivity analysis in which we restricted our analysis to those patients with at least a 5-year follow-up and an index examination after 2008, and observed similar results to the total sample: USMSTF 3-year group 11.9 %; 3–5-year group 13.3 %; 5–10-year group 10.4 %; 7–10-year group 7.3 %, and 10-year group 5.3 %.

The long-term risk for CRC detected on all subsequent colonoscopies including the first surveillance examination is shown in Table 4. The incidence of CRC per 100000 person-years was highest in the USMSTF 3-year group (3.54, 95 %CI 2.68–4.68) and the ESGE high risk group (3.43, 95 %CI 2.57–4.59). ESGE high risk (HR 3.03, 95 %CI 1.97–4.65) and USMSTF 3-year designations (HR 3.07, 95 %CI 2.03–4.66) were more likely to predict CRC compared with the other groups.

Discussion

In our analyses, we compared the ability of the high risk groups within the guidelines to predict the metachronous risk for the combined outcome of large (> 1 cm) serrated polyps, advanced adenomas, and CRC. To examine the impact of each index category on metachronous risk for neoplasia, we also examined the subcategories of the primary combined outcome: CRC and advanced adenoma on the one hand and large (> 1 cm) or dysplastic serrated polyps on the other. While the risk posed by conventional adenomas at index examination is typically understood as the specific risk of future advanced adenomas

or CRC, past work by our group and other researchers has shown that the risk posed by index serrated polyps is better understood relative to future large serrated polyps, not future conventional adenomas [4, 5]. In other words, the appropriate way to measure the risk posed by an index polyp is to look at the likelihood of developing future advanced polyps in the same pathway. In addition, we examined the long-term risk for CRC.

As patients present with polyps in both pathways, our combined outcome is the clinically relevant end point. Of note, only 20.6 % (505/2450) of patients in the ESGE high risk group had only advanced serrated polyps. Our results showed that the PPV and NPV for all outcomes were almost identical between the ESGE high risk and USMSTF 3-year categories, suggesting similar discriminating ability in predicting the combined outcome of metachronous advanced adenomas/CRC and large (> 1 cm) or dysplastic serrated polyps. The low discriminating abilities for ESGE and USMSTF (high risk group) recommendations were manifested in the relatively high metachronous risk for advanced neoplasia in the low risk groups of both guidelines and the respective modest odds ratios (OR; about twofold) in the regression models. The low PPVs further suggest that the guidelines from both societies may need to be further adjusted [6]. One potential alteration could involve the addition of some lower USMSTF risk groups to increase the yield of metachronous advanced neoplasia. However, our data suggest that if some lower risk USMSTF groups were added to the high risk category, or perhaps even to the ESGE group, the 3–5-year and 5–10-year groups in particular, the impact on NPV, PPV and number needed to diagnose would be minimal; when adding these lower risk USMSTF groups to the USMSTF 3-year group, the ORs rose only slightly, suggesting a minimal increase in discriminative ability of the new high risk group. Another important factor to consider when adding the 3–5-year and 5–10-year groups to the USMSTF 3-year group is the additional number of individuals who would undergo surveillance without high risk findings. Although we would identify 180 more individuals with metachronous neoplasia, an additional 1313 individuals would undergo surveillance colonoscopy without high risk findings, suggesting that there would be no benefit for these individuals by being in the high risk group.

ESGE ranks CRC incidence as a more relevant outcome than the risk for metachronous advanced neoplasia when estimating the benefit of post-polypectomy surveillance. Although CRC is a more important outcome to assess the long-term success of polyp surveillance paradigms, intermediate end points such as conventional advanced adenomas and large or dysplastic serrated polyps are common metachronous outcomes, as opposed to CRC. These more common intermediate outcomes can increase the power for investigation of important questions such as the risk of index small vs. diminutive adenomas or the risk of small (5–9mm) proximal HPPs [5,7].

When evaluating the long-term CRC outcomes, our results showed that the higher risk groups (ESGE high risk and USMSTF 3-year group) unsurprisingly were associated with a higher risk for CRC than the other categories. The incidence of CRC per 100 000 person-years was highest in the USMSTF 3-year group (3.54, 95 % CI 2.68–4.68) and the ESGE high risk group (3.43, 95 % CI 2.57–4.59). These data suggest that with respect to the long-term risk for CRC, the high risk 3-year USMSTF group and the high risk ESGE group are similar. As shown in Table 4, adding other USMSTF categories increased the number of

patients with CRCs correctly classified as high risk; however, it also increased the potential number of patients exposed to the risks associated with colonoscopy.

An interesting finding was that the risk for future large or dysplastic serrated polyps was higher in the 5–10-year group (10.0 %) than in all of the other groups including the USMSTF 3-year group. This is due to the inclusion of patients with only 1–2 SSPs in this category compared with the USMSTF 3-year group, which included patients with other nonserrated findings such as high risk conventional adenomas and no serrated polyps. Of note, the addition of the 1–2 small SSPs also increased the risk for metachronous advanced adenomas. In the 1–2 small (< 1 cm) SSP group, nearly a third of all patients had 1–2 small adenomas (134/400), demonstrating the important clinical observation that polyps of both types are commonly found at the same time.

For adenomas, the main difference between the ESGE and USMSTF high risk groups is that villous adenomas are considered high risk in the USMSTF guidelines, but are considered low risk in the ESGE guidelines unless the polyp is ≥ 1 cm. We found that the USMSTF 3-year group, which includes villous adenomas, had the highest absolute risk for metachronous advanced adenomas out of all USMSTF risk groups, at 9.0 %; similarly, the ESGE high risk group had an absolute risk for future advanced adenomas of 8.6 %, higher than the ESGE low risk group. Both ESGE high risk group (OR 2.18; $P < 0.0001$) and the USMSTF 3-year group (OR 2.19; $P < 0.001$) had significantly higher metachronous risks for all colorectal neoplasia than their respective low risk groups. Furthermore, the PPV and NPV for the combined outcome were almost identical for the USMSTF 3-year and ESGE high risk groups, suggesting that incorporation of villous histology may not be important in predicting-metachronous neoplasia. Notably, the previous ESGE guideline included villous histology; however, it was excluded from the updated guideline based on prior studies showing that villous histology was not an independent risk factor for long-term CRC [8–10]. Other reasons provided by the ESGE for not including villous histology as high risk included the low risk of HGD in villous adenomas < 1 cm, as well as the variation in pathologic interpretation of villous adenomas [2, 11]. In addition, the guidelines cite two studies, which observed that villous histology was not associated with an increased risk for CRC incidence or mortality, as well as a meta-analysis and a pooled analysis that showed that patients with villous adenomas had a risk for advanced neoplasia similar to that of controls [8–10, 12, 13].

Our study is the first to compare the 2020 USMSTF and ESGE guidelines for advanced adenoma, large serrated polyp, and CRC outcomes. Strengths of our study include the large sample size and the exclusion of incomplete colonoscopies and those with poor bowel preparation. Limitations of our study include its reliance on data from one US state with limited racial diversity, although New Hampshire does have considerable range in terms of ethnic and socioeconomic factors [14]. Future studies should incorporate data from other states with more racially diverse populations. Another limitation was that the intervals observed in our sample may have been different from the current USMSTF as the endoscopists may have been following older guidelines published in 2012 [15]. For example, the low risk adenomas had a recommended follow-up interval of 5–10 years. This is consistent with the mean follow-up time of approximately 5 years in the 7–10-year group.

In summary, our data suggest that both guidelines perform similarly in predicting metachronous advanced neoplasia. Therefore, differences such as attention to villous histology and subtypes of serrated polyps may not be as clinically relevant as initially thought. While the ESGE classifies 88.0 % (18 008/20458) of all examinations as low risk, the USMSTF classifies 54.9 % (11 226/20458) as low risk. Therefore, a large additional percentage (33.2 %; 6782/20458) would have no follow-up colonoscopies for at least 10 years under the ESGE classification. The simplicity of two groups in the ESGE classification may be associated with higher compliance.

We also observed risks of 5.1 % and 6.3 % for metachronous advanced neoplasia in the USMSTF and ESGE guideline low risk groups, respectively, likely due to the low discriminative ability of both guidelines. Whereas the low risk groups had longer follow-up times than the higher risk groups, the relatively high risks do highlight the need to establish an acceptable cutoff risk for metachronous neoplasia in patients who will wait 10 years for the recommended follow-up colonoscopy. In the USMSTF guideline, more patients with CRC or advanced neoplasia would be diagnosed on a surveillance colonoscopy < 10 years. However, even in the USMSTF guideline, where the focus is on polyps and CRC prevention, a large proportion of patients (38.6 %; 569/1474) with metachronous advanced neoplasia would still wait 10 years for the recommended follow-up based on our sample. Ultimately, the decision for surveillance paradigms is based on the choice of outcomes. Using intermediate outcomes such as metachronous advanced polyps might capture more patients at high risk. However, this strategy would require more surveillance examinations compared with using CRC prevention as an end point, which would require fewer colonoscopies. Further investigation and consideration are needed into how the guidelines can be modified to maximize CRC prevention with colonoscopy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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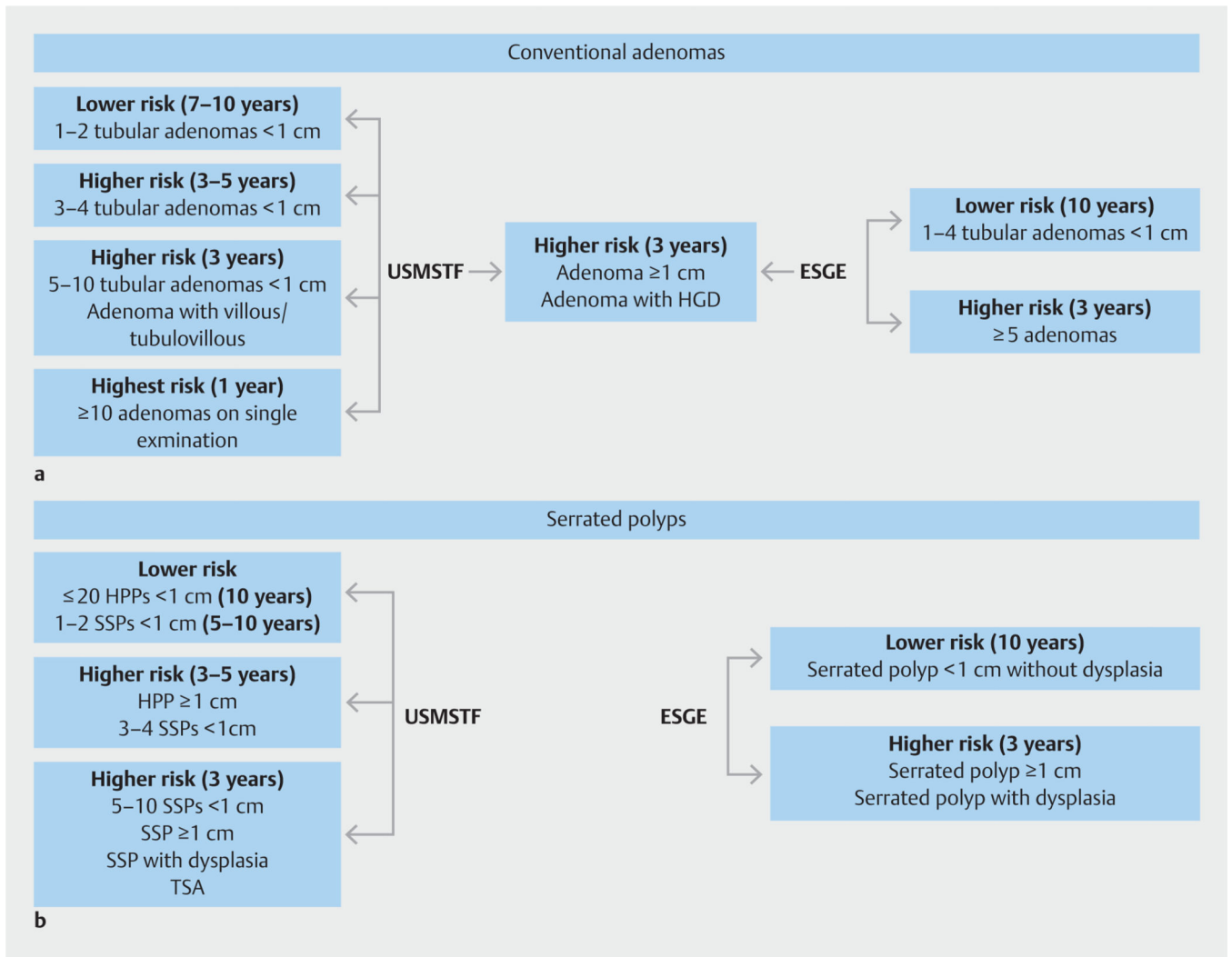


Fig.1. Risk groups for serrated polyps and conventional adenomas as classified by the US Multi-Society Task Force on Colorectal Cancer (USMSTF) and European Society of Gastrointestinal Endoscopy (ESGE). **a** Conventional adenomas. **b** Serrated polyps. HGD, high grade dysplasia; HPP, hyperplastic polyp; SSP, sessile serrated polyp; TSA, traditional serrated adenoma.

Table 1

Patient demographics and examination characteristics as stratified by the US Multi-Society Task Force on Colorectal Cancer (USMSTF) and European Society of Gastrointestinal Endoscopy (ESGE) guideline categories based on index examination findings.

	USMSTF recommendations					ESGE recommendations	
	USMSTF 10 year low risk (n = 11/226)	USMSTF 7-10 year (n = 5222)	USMSTF 5-10 year (n = 400)	USMSTF 3-5 year (n = 1093)	USMSTF 3 year (n = 2517)	ESGE (n = 18/008)	ESGE (n = 2450)
	No adenomas HPPs (< 1 cm)	1-2 tubular adenomas < 1 cm	1-2 SSPs < 1 cm	3-4 tubular adenomas < 1 cm, HPP 1 cm, 3-4 SSPs < 1 cm	5-10 tubular adenomas < 1 cm, adenoma 1 cm or villous/tubulovillous or HGD, SSP 1 cm or with dysplasia, TSA or 5-10 SSPs	Low risk 0-4 adenomas < 1 cm, all serrated polyps without dysplasia < 1 cm	High risk Adenomas 1 cm or HGD, 5 adenomas, serrated polyps 1 cm or with dysplasia
Follow-up, mean (SD), months	75.4 (32.5)	58.9 (19.1)	47.4 (18.7)	46.3 (20.2)	39.3 (20.8)	68.1 (29.9)	39.4 (21.1)
Bowel preparation quality, % Fair (n)	9.1 (1023)	9.1 (476)	5.3 (21)	11.0 (120)	9.1 (228)	9.0 (1629)	9.8 (239)
Age, mean (SD), years	58.7 (7.8)	59.8 (8.1)	58.4 (8.1)	62.1 (8.4)	60.91 (8.6)	59.2 (8.0)	60.7 (8.5)
Male sex, % (n/N)	41.5 (4648/11212)	55.8 (2915/5221)	44.5 (178/400)	66.1 (722/1092)	58.9 (1483/2516)	47.3 (8512/17992)	58.6 (1434/2449)
BMI, mean (SD), kg/m ²	27.9 (5.8)	28.6 (5.8)	28.3 (5.81)	29.8 (6.52)	29.1 (6.11)	28.2 (5.8)	29.1 (6.3)
Current smoker, % (n/N)	6.9 (741/10790)	9.1 (459/5049)	12.6 (49/389)	11.6 (122/1055)	15.1 (363/2409)	7.9 (1362/17343)	15.8 (372/2349)
Family history of CRC in first-degree relative, % (n/N)	13.5 (1380/10212)	10.0 (496/4964)	10.0 (39/389)	9.5 (101/1066)	8.7 (212/2440)	12.0 (2003/16685)	9.4 (225/2386)

HPP, hyperplastic polyp; SSP, sessile serrated polyp; HGD, high grade dysplasia; TSA, traditional serrated adenoma; BMI, body mass index; CRC, colorectal cancer.

Table 2

Unadjusted risk for significant metachronous neoplasia (colorectal cancer, advanced adenomas, large or dysplastic serrated polyps) on first surveillance colonoscopy for each US Multi-Society Task Force on Colorectal Cancer (USMSTF) and European Society of Gastrointestinal Endoscopy (ESGE) category compared with the low risk category (10-year low risk group for US categories).

	USMSTF recommendations					ESGE recommendations		
	Low risk USMSTF 10 year (n = 11 226)	USMSTF 7-10 year (n = 5222)	USMSTF 5-10 year (n = 400)	USMSTF 3-5 year (n = 1093)	USMSTF 3 year (n = 2517)	ESGE (n = 18/008)	ESGE (n = 2450)	
	US Reference No adenomas HPPs (all < 1 cm)	1-2 tubular adenomas < 1 cm	1-2 SSPs < 1 cm	3-4 tubular adenomas < 1 cm, HPP 1 cm, 3-4 SSPs < 1 cm	5-10 tubular adenomas < 1 cm, adenoma 1 cm or villous/tubulovillous or HGD, SSP 1 cm or with dysplasia, TSA or 5-10 SSPs	Low risk 0-4 tubular adenomas < 1 cm, all serrated polyps < 1 cm or without dysplasia	High risk Adenomas 1 cm or HGD, 5 adenomas, serrated polyps 1 cm or with dysplasia	
All 3 outcomes (advanced adenomas, large serrated polyps, CRC), % (95 %CI) (n)	5.1 (4.7-5.5) (569) Reference	7.4 ¹ (6.7-8.1) (384)	13.5 ¹ (10.5-17.2) (54)	11.5 ¹ (9.8-13.6) (126)	13.6 ¹ (12.3-14.9) (341)	6.3 (6.0-6.7) (1142)	13.6 ² (12.3-15.0) (332)	
Incidence per 1000 person-years (95 %CI)	8.08 (7.46-8.74)	15.01 (13.69-16.46)	34.37 (27.69-42.66)	30.01 (25.93-34.73)	41.74 (38.50-45.27)	11.20 (10.60-11.83)	41.67 (37.38-45.24)	
Sub outcomes, % (n)								
Advanced adenomas	2.8 (n313) Reference	5.1 ¹ (268)	4.0 ² (16)	7.6 ¹ (83)	9.0 ¹ (227)	3.9 (696)	8.6 ² (211)	
Large and dysplastic serrated polyps	1.9 (208) Reference	2.0 ⁴ (106)	10.0 ¹ (40)	3.5 ¹ (38)	4.3 ¹ (109)	2.1 (387)	4.7 ² (114)	
CRC	0.6 (62)	0.4 (21)	0.3 (1)	0.6 (7)	0.5 (13)	0.5 (89)	0.6 (15)	

HPP, hyperplastic polyp; SSP, sessile serrated polyp; HGD, high grade dysplasia; TSA, traditional serrated adenoma; CRC, colorectal cancer.

Please note that total numbers for sub outcomes are higher than total due to patients having more than one outcome.

¹ $P < 0.001$ for comparison with reference (negative examination) group unless noted.

² $P < 0.0001$

³ $P = 0.15$.

⁴ $P = 0.52$

Table 3

Comparison of European Society of Gastrointestinal Endoscopy (ESGE) versus US Multi-Society Task Force on Colorectal Cancer (USMSTF) guidelines for metachronous advanced colorectal neoplasia (advanced adenoma/CRC and large or dysplastic serrated polyps combined) with positive and negative predictive values and number needed to diagnose.

	Index polyps included		PPV, % (95 %CI) (n/N)	NPV (95 %CI) (n/N)	Number needed to colonoscope	OR (95 %CI) ^f
ESGE	High risk Adenomas 1 cm or HGD, 5 adenomas, serrated polyps 1 cm or with dysplasia	Low risk 1–4 tubular adenomas < 1 cm, all serrated polyps < 1 cm or without dysplasia	13.6 (12.3–15.0) (332/2450)	93.7 (93.3–94.0) (16866/18008)	7	2.18 (1.88–2.52)
USMSTF 3	High risk 5–10 tubular adenomas < 1 cm, adenoma 1 cm or villous/tubulovillous or HGD, SSP 1 cm or with dysplasia, TSAs	Low risk 3–4 tubular adenomas < 1 cm, HPP 1 cm, 3–4 SSPs < 1 cm, 1–2 SSPs < 1 cm, 1–2 tubular adenomas < 1 cm, HPPs < 1 cm	13.6 (12.3–14.9) (341/2517)	93.7 (93.3–94.0) (16808/17941)	7	2.19 (1.89–2.52)
USMSTF 3 and 3–5	High risk Above + 3–4 tubular adenomas < 1 cm, HPP 1 cm, 3–4 SSPs < 1 cm	Low risk 1–2 SSPs < 1 cm, 1–2 tubular adenomas < 1 cm, HPPs < 1 cm	12.9 (11.9–14.1) (467/3610)	94.0 (93.7–94.4) (15/841/16/848)	8	2.21 (1.94–2.53)
USMSTF 3, 3–5, and 5–10	High risk Above + 1–2 SSPs < 1 cm	Low risk 1–2 tubular adenomas < 1 cm, HPPs < 1 cm	13.0 (12.0–14.1) (521/4010)	94.2 (93.8–94.6) (15/495/16/448)	8	2.36 (2.07–2.69)
USMSTF 3, 3–5, 5–10, and 7–10	High risk Above + 1–2 tubular adenomas < 1 cm	Low risk HPPs < 1 cm	9.8 (9.2–10.4) (905/9232)	94.9 (94.5–95.3) (10/657/11/226)	10	1.96 (1.73–2.22)

PPV, positive predictive value; NPV, negative predictive value; OR, odds ratio; HGD, high grade dysplasia; SSP, sessile serrated polyp; TSA, traditional serrated adenoma; HPP, hyperplastic polyp

^fResults of multivariable logistic regression adjusting for age, sex, body mass index, and months to follow-up.

Table 4

Long-term risk of colorectal cancer on all subsequent colonoscopies (after index and first surveillance examinations).

		No. of colonoscopies	Unadjusted CRC risk for patients on any follow-up examination, % (95%CI) (n) ¹	Time to surveillance examination, mean (SD), months	Time to CRC diagnosis, mean (SD), months	Incidence per 100 000 person-years, (95 %CI)	HR (95 %CI) ²
ESGE	High risk	3089	1.0 (0.7–1.4) (30)	34.0 (22.9)	35.9 (30.5)	3.43 (2.57–4.59)	3.03 (1.97–4.65)
	Low risk	19/499	0.6 (0.5–0.8) (123)	65.8 (31.2)	55.8 (32.9)	1.15 (0.97–1.36)	1.0 (Reference)
USMSTF 3	USMSTF 3	3182	1.0 (0.7–1.4) (32)	34.1 (22.7)	29.6 (26.5)	3.54 (2.68–4.68)	3.07 (2.03–4.66)
	USMSTF 3, 3–5, 5–10, 7–10 and 10	19/406	0.6 (0.5–0.7) (121)	66.0 (31.2)	57.8 (32.6)	1.13 (0.96–1.34)	1.0 (Reference)
USMSTF 3, 3–5	USMSTF 3, 3–5	4373	0.9 (0.7–1.3) (41)	36.9 (22.8)	35.2 (30.9)	3.05 (2.36–3.93)	2.55 (1.73–3.77)
	Reference	18/215	0.6 (0.5–0.7) (112)	67.4 (31.2)	58.0 (32.2)	1.10 (0.92–1.30)	1.0 (Reference)
USMSTF 3, 3–5, 5–10	USMSTF 3, 3–5, 5–10	4809	0.9 (0.7–1.2) (42)	37.6 (22.7)	34.9 (30.7)	2.79 (2.16–3.60)	2.36 (1.60–3.48)
	Reference	17/779	0.6 (0.5–0.8) (111)	67.9 (31.2)	58.3 (32.2)	1.10 (0.93–1.31)	1.0 (Reference)
USMSTF 3, 3–5, 5–10, 7–10	USMSTF 3, 3–5, 5–10, 7–10	10/403	0.6 (0.5–0.8) (67)	48.4 (23.8)	39.9 (27.2)	1.60 (1.28–1.99)	1.26 (0.88–1.79)
	Reference	12/185	0.7 (0.6–0.9) (86)	72.6 (34.0)	61.2 (34.8)	1.17 (0.96–1.42)	1.0 (Reference)

CRC, colorectal cancer; HR, hazard ratio; ESGE, European Society of Gastrointestinal Endoscopy; USMSTF, US Multi-Society Task Force on Colorectal Cancer

¹Numbers of CRCs are greater than those in Table 2 due to inclusion of examinations 3 month or longer after index (versus 12 months), as well as CRCs diagnosed on colonoscopies after first surveillance examination.

²Results of Cox's proportional hazards models adjusting for age, sex, year of examination, bowel preparation, and having more than one surveillance examination.