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Does Colon Polyp Surveillance Improve Patient Outcomes?

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Abstract

Colon polyp surveillance now accounts for 25% of all colonoscopies performed. The evidence that colonoscopy surveillance reduces colorectal cancer (CRC) incidence or mortality is weak. The biology of the baseline lesions and quality of the baseline exam are two primary factors contributing to post-colonoscopy CRC. Prior recommendations for surveillance were based largely on the likelihood that patients with adenomas would develop advanced adenomas, a surrogate for CRC. There is now evidence that baseline colonoscopy findings are strongly associated with the risk of incidence or death from CRC. This evidence provides a basis for updated evidence-based recommendations for surveillance. In addition, there is also growing evidence that the quality of the baseline exam is an important predictor of the likelihood of developing post-colonoscopy CRC.

Summary

Since the 2012 colon polyp surveillance recommendations, there is now stronger evidence for risk stratification based on the characteristics of polyps at the baseline colonoscopy. It is very clear that quality of the baseline examination is a key determinant of post-polypectomy CRC risk. As endoscopists improve the quality of colonoscopy, it is reasonable to expect that the rate of post-colonoscopy CRC may decline for most individuals with polyps, and that surveillance can be focused primarily on high-risk individuals.

Keywords

Colon Polyp; Colorectal Cancer; Colonoscopy; Colon Polyp Surveillance

There is now substantial evidence that colorectal cancer (CRC) screening is effective: that a successful screening program can be implemented, and can result in reduced CRC mortality and incidence.[1] The additional benefits of surveillance after baseline screening colonoscopy

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Conflicts of interest

The authors disclose no conflicts.

are less clear, and are reviewed herein. The Multi-Society Task Force on CRC published recommendations for follow-up after detection and removal of polyps[2] and CRC.[3] New polyp surveillance recommendations were published in 2020,[4] based on a review of new evidence since 2012. We summarize the most current evidence that informed the 2020 recommendations.

History of Polyp Surveillance

CRC screening is best viewed as a program that can lead to colonoscopy, discovery of cancer or precancerous polyps, and identification of high-risk individuals who may benefit from follow-up after colonoscopy. In contrast to CRC screening, there is almost no evidence that supports the effectiveness of colonoscopy surveillance for reduction of CRC incidence and mortality. In fact, it is entirely possible that a high-quality initial baseline colonoscopy, with detection and removal of polyps, provides protection against subsequent cancer, and that surveillance may have very little added effect. Surveillance now accounts for approximately 25% of all colonoscopies in the United States.[5] Why do we do it if we lack evidence? The answer is based on a simple postulate: patients who form adenomas or develop cancer have whatever it takes (genetics, lifestyle or environment factors) to develop colon neoplasia, and they may do it again.

The history of surveillance informs the current recommendations for follow-up after colonoscopy.

1. Risk stratification. The risk of CRC after detection of adenomas is derived from several lines of evidence. The first major study found that among patients who had sigmoidoscopy, individuals with small (<10 mm) tubular adenomas had a low risk of subsequent CRC, whereas patients with large (>10 mm) adenomas or adenomas with villous histology had an increased risk of CRC.[6] Subsequent studies demonstrated that individuals with a high-risk adenoma (HRA) defined as an adenoma >10 mm, or with villous histology or highgrade dysplasia, had a higher risk of developing more HRAs during follow-up compared with those with low-risk adenomas (LRAs), defined as 1 to 2 tubular adenomas <10 mm.[7] The use of HRA as a surrogate for CRC is based on an assumption that individuals with HRAs are more likely to develop CRC compared with those with LRA. It is an imperfect surrogate that may be predictive only of future HRA, not CRC.

2. Interval for surveillance. In 1993, the National Polyp Study reported no benefit to a 1-year examination after adenoma removal, and surveillance intervals were extended for most individuals to 3 years.[8] Over time, more studies with 3- to 5-year follow-up after baseline colonoscopy used the HRA as a surrogate endpoint of risk, which has led to longer recommended intervals.[2,7]

By 2012, a robust body of literature demonstrated a close relationship between baseline colonoscopy findings and the risk of HRA (not CRC) during surveillance.[2] In addition, there were several studies that clarified the risk of HRA during serial surveillance (i.e., the second and third colonoscopy after the baseline examination). Data on the follow-up of sessile

serrated polyps (SSP) were considered for the first time, although evidence of outcomes was weak. All of these recommendations were based on the surrogate endpoint of HRA, because few studies had a CRC endpoint that could be analyzed.

Summary of New Evidence With CRC Outcomes

Several studies since 2012 report the risk of CRC incidence and/or mortality endpoints after colonoscopy, which provide evidence for the 2019 recommendations. Key studies include the following:

1. A large cohort study of more than 300,000 individuals with normal colonoscopy showed a reduced risk for incident CRC (hazard ratio 0.44), which was durable for at least 15 years.[9]

2. Another cohort study from the United States found a 46% reduced risk for incident CRC, and 88% relative reduced risk for fatal CRC among nearly 100,000 with a normal colonoscopy.[10]

3. A Norwegian cohort study[11] of more than 40,000 subjects with adenomas removed found that the risk for fatal CRC was decreased by 25% for patients with LRA (compared with the general population). Individuals with HRAs had a higher risk of fatal CRC compared with the general population (standardized mortality ratio 1.2 [1.02–1.31]). These data support the recommendation that individuals with LRA are a lower than average risk group who do not need intensive surveillance, and provide stronger evidence for surveillance of individuals with HRA at baseline colonoscopy.

4. Individuals who participated in the US trial of sigmoidoscopy screening were followed over time[12] to determine rates of fatal CRC. Compared with those with no neoplasia, the risk for incident and fatal CRC was increased among participants with HRA (RR 2.7 for incident CRC and 2.6 for fatal CRC) but similar for those with LRA (RR 1.2 for incident CRC and fatal CRC). These data demonstrate the favorable outcomes of patients with LRA. A challenge in interpreting this study is that a large proportion received at least one surveillance colonoscopy (78.1% and 69.9% at 9 years' follow-up for the nonadvanced vs no adenoma groups, respectively), making it difficult to assess whether exposure to surveillance may have had a role in making the outcomes among patients with nonadvanced adenoma similar to those with no neoplasia.

5. There is new evidence that surveillance after polypectomy can reduce the risk of CRC. A study from the United Kingdom defined a group of patients with "intermediate" risk (based on having 1 to 2 adenomas ≥10 mm or 3 to 4 adenomas <10 mm in size) and showed that these patients had better outcomes with surveillance compared with a cohort without surveillance.[13] This is perhaps the most compelling evidence to date that surveillance of patients with specific findings at baseline (such as adenoma ≥10 mm) can reduce the risk of CRC.

6. There are now data that colonoscopy quality is an important risk factor for post-colonoscopy CRC, in addition to baseline findings.[14] Post hoc analyses of post-

colonoscopy CRC suggest that more than 50% of such cancers are likely the result of lesions missed at baseline.[15] Endoscopists with low adenoma detection rates (ADRs) have higher rates of interval CRC,[16] and with improvement in ADRs, interval cancer rates decline.[17] New data on incomplete resection of polyps[18] highlight the importance of careful assessment of polyps to ensure complete removal.

These studies with CRC outcomes are consistent with the earlier studies with HRA endpoints, and now provide stronger evidence for the 2020 surveillance recommendations (Table 1). The results confirm that the baseline findings are highly predictive of subsequent of CRC, and should be key determinants of surveillance intervals.

Status of Surveillance in 2019

There is now strong evidence that colonoscopy examination quality is a predictor of post-colonoscopy CRC. There is consensus that a high-quality examination should be defined as follows:

1. Complete examination to cecum with documentation
2. Adequate bowel prep to detect lesions >5 mm
3. High-quality endoscopist, meeting ADR benchmarks of 20% for women and 30% for men
4. Complete polyps resection with document polyp size

Low-Risk Patients

Compared with 2012, there is stronger evidence that individuals with no adenoma, or 1 to 2 small (<10 mm) tubular adenomas at baseline are very low-risk for developing CRC. This evidence supports the extension of the surveillance interval to more than 5 years. Prior work that polyp multiplicity (3+) is associated with a higher risk of HRA during surveillance comes from the 1990s in an era preceding high-definition endoscopy and quality metrics focused on adenoma detection. It is very likely that modernday high-detectors may now identify individuals with 3 to 4 small tubular adenomas with risk that might be similar to patients with 1 to 2 small adenomas.[19] In a cohort study[12] that compared long-term outcomes in patients with 3 or more nonadvanced adenomas with subjects who had 1 to 2 nonadvanced adenomas, there was no difference in incident CRC (RR 1.10) and the cumulative rate of advanced adenoma removal up to 9 years was similar (10.7% vs 7.1%). In an era of higher rates of adenoma detection, the finding of 3 to 4 small tubular adenomas may be a signal of procedure accuracy, and identify a low-risk individual. More evidence is needed to support this hypothesis.

High-Risk Patients

Based on CRC endpoints, individuals with HRA have a higher risk of developing CRC during surveillance and may benefit from more intensive surveillance, with initial examination at 3 years.

Serial Surveillance After the First Surveillance Examination

Several new studies since 2012[20-23] provide evidence of risk of HRA (not CRC) at a second surveillance examination. The most significant finding in these studies is that the detection of HRA, either at baseline or first surveillance examination, identifies individuals who continue to have a higher likelihood of HRA at a second surveillance examination.

Sessile Serrated Polyps

The prevalence of SSPs at screening colonoscopy may be 5% to 10%. Evidence for natural history of SSPs remains weak because of issues of misclassification by pathologists, failure of endoscopic detection, and studies that mix various large and small SSPs with conventional adenomas. The risk of CRC is clearly high in patients with serrated polyposis. Case-control and cohort studies since 2012[24,25] have shown that patients with large or dysplastic SSPs may also have increased risk for incident CRC. The largest cohort study[26] of 5433 individuals in which surveillance was performed, suggests that individuals with isolated SSPs and no conventional adenomas at baseline have a higher risk of having large SSPs, but a low risk of HRA during surveillance. Interestingly, the patients at highest risk for HRA appeared to be those with the combination of both baseline SSPs and conventional adenomas, although more studies are need to support this observation. We can conclude that SSPs are a risk factor for more SSPs, but the risk of CRC after detection and resection of SSPs remains uncertain. Although the evidence is weak, a cautious approach would be to consider 1 to 2 small SSPs as similar to LRAs, and larger SSPs or SSPs with dysplasia as similar to HRAs.

Utilization of Polyp Surveillance in Clinical Practice

The utilization of colon polyp surveillance is uncertain, and there is evidence for both under- and overutilization of surveillance, with a recent meta-analysis concluding that the average adherence to recommended surveillance colonoscopy intervals is less than 50%.[27] Few studies have followed patients longitudinally to determine adherence to current guidelines and ultimately whether surveillance in clinical practice reduces mortality.

Areas for Further Research

Our review of the literature identified several areas that require further research.

1. Importance of quality. There is evidence that as quality improves, the risk of CRC after colonoscopy is reduced.[17] Because higher quality presumably leads to better polyp detection, patients who have colonoscopy performed by colonoscopists with high ADRs may have more intense surveillance, despite being at lower risk for CRC compared with patients who have colonoscopy performed by colonoscopists with lower ADRs. As more endoscopists measure and improve quality in their practice, it is possible that the rates of missed lesions or incompletely removed lesions will decline, and intervals can be safely extended to avoid overaggressive surveillance.

2. Additional risk factors. Further research is needed to understand other potential risk factors that might influence CRC risk after a baseline colonoscopy, such as age of diagnosis of adenoma, gender, proximal vs distal adenoma, smoking, aspirin or nonsteroid antiinflammatory drug use, obesity, and family history of adenoma.

3. SSPs. There is little doubt that the SSP pathway is an important contributor to post-colonoscopy CRC, which is more likely to be in the proximal colon, have CPG island methylation, and microsatellite instability, compared with prevalent CRCs detected on first-time colonoscopy. We do not know if these interval CRCs with characteristics of the SSP pathway are due primarily to failure of detection at the baseline examination or biology that results in more rapid progression to CRC. Improvement in endoscopic detection and pathology classification will help clarify the natural history of SSPs. Further, future research should clarify whether patients with both conventional adenomas and SSPs represent a particularly high-risk group.

4. The role of intermediate testing. There is evidence that most post-colonoscopy CRCs occur in the first years after colonoscopy, which may be because of lesions missed or incompletely removed at baseline. These are quality issues, which may improve with the recognition and measurement of quality in endoscopy. Colonoscopy is an imperfect art, and it is possible that supplementation with a noninvasive test (such as fecal immunochemical test [FIT], fecal FIT/ DNA, or other biomarker) could improve the outcomes of surveillance. Further study is needed to test this hypothesis.

5. Longitudinal follow-up after baseline colonoscopy is needed to understand whether adherence to recommendations improves patient outcomes.

6. Effectiveness of surveillance. Additional research is needed to clarify whether exposure to surveillance colonoscopy after polypectomy consistently reduces CRC incidence and mortality, and which patients are most likely to benefit.

Biography

Abbreviations used in this paper:

ADRs	adenoma detection rates
CRC	colorectal cancer
HRA	high-risk adenoma
LRAs	low-risk adenomas
SSP	sessile serrated polyps

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Table 1.

Summary of New Evidence for Colon Polyp Surveillance Since 2012

Colonoscopy surveillance category	Evidence
Baseline colonoscopy results	
1. No neoplasia	Two large cohort studies demonstrate a reduced risk for incident CRC (HR 0.44) and mortality (0.12) after a normal colonoscopy.[9,10] This reduction in risk is durable for at least 10 years.
2. LRA: stronger evidence that this is a low-risk group	a. Cohort study[11]: fatal CRC was decreased by 25% in patients with LRA compared with the general population, suggesting that this is a low-risk group
	b. US sigmoidoscopy study[12] followed over time. Patients with LRA had RR of 1.2 for incident CRC compared with patients with no neoplasia
3. HRA: stronger evidence that this is a high-risk group, and benefits from colonoscopy surveillance	a. Cohort study[11]: individuals with HRA had higher risk of fatal CRC compared with general population
	b. US sigmoidoscopy study[12]: HRA associated with higher risk of incident and fatal CRC c. UK study[13]: individuals with HRA had reduced risk of CRC if they had surveillance compared with those who had no surveillance
4. SSPs	Evidence weak. There is growing evidence that having baseline SSPs is a predictor of detecting large SSPs during surveillance[24-26]
Colonoscopy surveillance after the first surveillance examination	New evidence that the finding of an HRA at baseline, or at the first surveillance examination, is associated with a higher risk of detecting HRAs on subsequent surveillance examinations[20-23]

CRC, colorectal cancer; HR, hazard ratio; HRA, high-risk adenoma; LRA, low-risk adenoma; RR, relative risk; SSP, sessile serrated polyp.

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