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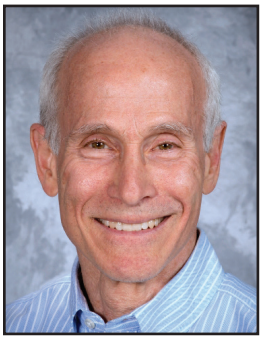
Update on Colon Polyp Surveillance



David Lieberman

The benefits of surveillance colonoscopy after removal of adenomas have been uncertain. Recommendations for surveillance intervals have previously relied on studies which determined the risk of advanced adenomas after colonoscopy, as a surrogate of colorectal cancer (CRC). Over the past few years, new studies with CRC endpoints have emerged. The evidence that high-risk adenomas (defined as adenomas >10mm, or with villous histology or high-grade dysplasia) are associated with a high risk of CRC during surveillance is strong. These are individuals most likely to benefit from surveillance colonoscopy at relatively short intervals. Low-risk adenomas (defined as 1-2 tubular adenomas <10mm) are associated with a low risk of CRC, which is similar to the risk in patients with no adenomas. These patients may not need surveillance. New recommendations highlight the importance of a high-quality baseline exam as the cornerstone of surveillance interval recommendations.

INTRODUCTION

Colon polyp surveillance is part of the colorectal cancer (CRC) screening continuum. As more patients are screened, more adenomas are detected and surveillance is recommended. This results in a large burden of colonoscopy. The basis for follow-up after polyp removal dates back to the discovery of mutations associated with adenoma and serrated polyp formation that can, with additional mutations, evolve into cancer. However, most polyps are not destined to become CRC – in fact 40-60% of average risk individuals develop adenomas in their lifetime, and only 5% develop CRC. Most adenoma-bearing patients have only low-risk adenomas (LRA) defined as 1-2 tubular adenomas <10mm, and there is growing evidence that the risk of CRC in such patients is low. Therefore, many patients undergoing surveillance are unlikely to benefit.

Colon surveillance recommendations after polypectomy from 2012[1] were based largely on the risk of developing high-risk adenomas (HRA), defined as adenomas >10mm, or with villous histology or high-grade dysplasia, during follow-up after a baseline colonoscopy. HRA were used as a surrogate of CRC, since so few studies had CRC endpoints. New evidence has emerged in the past two years, which provides long-term follow-up of large cohorts, which assess the risk of developing CRC after polypectomy. This new

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information informs 2020 recommendations from the US Multi-Society Task Force (USMSTF) on CRC.[2] In addition to understanding how the biology of polyps detected at the initial baseline colonoscopy impacts subsequent CRC risk, there is also increased awareness of the impact of the colonoscopy quality on the risk of CRC after colonoscopy. This review will focus on this new data.

Why Should Surveillance be Considered?

It would be wonderful if a single colonoscopy eliminated the risk of CRC, but that is not the case. The true risk of post-colonoscopy CRC is uncertain. Cancer registry studies look back at a cohort with CRC and ask: how many of these patients had a colonoscopy within three years in which cancer was not diagnosed? The answer is 2-9%, with the most recent study from a Danish registry with over 10,000 CRCs finding that 7% had prior colonoscopy.[3] This does not prove that surveillance will necessarily confer benefit, but it establishes that CRC does develop after colonoscopy – either related to biology, quality of the baseline exam or both.

Biology: Risk of CRC After Removal of LRA and HRA

There is new evidence establishing the risk of CRC after polypectomy depending on the baseline findings (Table 1). Combined, these studies reveal that individuals with baseline HRA have a 2 to 4 fold increased risk of CRC during follow-up, compared to individuals with LRA or no adenomas.[4-6] This finding confirms the relevance of HRA, and justifies an intensive regimen of surveillance for individuals with HRA. For individuals with LRA, the risk is similar to those with no adenomas, and therefore, the benefits of surveillance are less clear. These patients account for more than 65% of adenoma-bearing patients, representing a substantial colonoscopy burden. The lower risk is reflected in the USMSTF recommendations for less intensive surveillance (7-10 year interval). It is entirely possible that such patients could be re-entered into routine screening after 10 years and enjoy a similar benefit as surveillance.[7]

In addition to standard adenomas, there is growing evidence of the importance of the sessile serrated polyp (SSP) pathway in the development of CRC. This pathway may account for 10 to 15% of CRCs. In the spectrum of post-colonoscopy CRC, features of the SSP pathway are twice as common compared to CRCs discovered at baseline exam. Li et al.[8] found that SSPs >10mm were associated with a significantly higher risk of CRC within 3-5 years, compared to individuals with small proximal or distal SSPs. Therefore these lesions should be managed like classical HRA with a three year interval for surveillance.[2] Table 2 provides summary of the USMSTF recommendations.

What about continued surveillance after the first surveillance exam? Five relevant studies were reviewed by USMSTF,[2] and the consistent conclusion was that the presence of a HRA either at baseline or during the surveillance period identified a high-risk individual. The data do not include studies with CRC endpoints, so this "high" risk refers to the risk of developing more HRA.

Table 1. Risk of Incident CRC After Baseline Colonoscopy - New Studies in 2020

Study	Follow-up	Incident CRC (baseline findings)		
		No adenoma	LRA	HRA
He; 2020[4]	10 years	0.4% 427/112/107	0.32% 12/3708	1.6% 39/2453
Wieszcsy; 2020[5]	7.1 years	0.16% 309/194,311	0.22% 58/26,536	0.47% 72/15,242
Lee; 2020[6]	8.1 years	0.25% 117/45,881	0.34% 37/10,978	0.8% 60/7563

Legend: 3 new studies with long-term follow-up of patients after colonoscopy

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Nevertheless, when combined with the new data about HRA noted above, intensive follow-up is likely to be beneficial if patients have HRA at some point in the surveillance continuum. These recommendations are summarized in Table 3.

Impact of Quality on Surveillance

Over the past few years, there has been growing evidence that quality of the baseline colonoscopy impacts post-colonoscopy outcomes. Corley et al.[9] demonstrated an inverse correlation between adenoma detection rate (ADR) and risk of post-colonoscopy CRC. Kaminski et al.[10] found a similar inverse relationship, and also showed that if ADR was improved, rates of post-colonoscopy CRC declined. Lam et al.[11] confirm this inverse relationship between ADR and post-colonoscopy CRC incidence occurring within 36 months and also 60 months of the baseline exam.

What about CRC mortality? A new study[12] found a strong relationship of overall quality (defined by cecal intubation, bowel prep and ADR) on both CRC incidence and mortality of post-colonoscopy patients. Both CRC incidence and mortality were two-fold higher in patients receiving low quality colonoscopy compared to high-quality colonoscopy.

In addition to polyp detection, complete polyp resection is another element of quality. A new meta-analysis[13] found that there was residual neoplastic tissue detected after 16-21% of polypectomies, and it is likely that this may underestimate the true rate of incomplete resection in clinical practice.

These studies confirm that quality matters, and impacts post-colonoscopy outcomes. The USMSTF recommendations acknowledge this effect by placing quality as the cornerstone of the recommendations (Table 2). High quality is defined as a complete exam to the cecum, with an adequate bowel prep (to detect lesions >5mm), complete polyp resection, performed by an endoscopist with demonstrated adequate ADR of 20% in women, 30% in men.[2]

Does Surveillance Colonoscopy Reduce CRC Incidence or Mortality?

There has been a long-standing belief that the

Table 2. Summary of USMSTF 2020 Colon Polyp Surveillance Recommendations[2]

Baseline Colonoscopy	Recommendations based on high quality baseline exam defined by: Complete exam to cecum; Adequate bowel prep to detect lesions >5mm Adequate Endoscopist ADR Complete complete polyp resection
Baseline Findings	**Surveillance Interval Recommendations**
No neoplasia	10 years
1-2 Tubular Adenomas <10mm	7-10 years
3-4 Tubular Adenomas <10mm	3-5 years
SSP 1-2 <10mm	5-10 years
SSP 3-4 <10mm	3-5 years
High Risk Tubular adenoma or SSP ≥10mm 5-10 adenomas or SSPs Adenoma with Villous histology Adenoma with HGD SSP with dysplasia or traditional	3 years
10+ adenomas	1 year

Legend: Polyp surveillance recommendations adapted from Gupta et al.[2]

Table 3. Serial Surveillance Colonoscopy (adapted from Gupta 2020)

Baseline Exam	Follow-up (yrs)	Surveillance #1	Recommended interval (yrs)	Future interval after (-) Surveillance #1
1-2 TA <10mm	7-10 yrs	Normal	10	10
		1-2 TA <10mm	7-10	10
		3-4 TA <10mm	3-5	10
		HRA*	3	5
HRA*	3	Normal	5	5
		1-2 TA <10mm	5	5
		3-4 TA <10mm	3-5	5
		HRA*	3	5

HRA* defined as tubular adenoma(s) >10mm, or with villous histology or high-grade dysplasia
Legend: Follow-up of patients after the first colonoscopy surveillance, adapted from Gupta et al.[2]

greatest benefit of colonoscopy is derived from the baseline exam, when polyps are detected and removed. The demonstration that surveillance impacts key outcomes such as CRC incidence and mortality is uncertain. These studies would require large cohorts with very long-term follow-up. Decision models often fill in gaps where data is lacking. A new model[7] suggests that intensive surveillance for HRA at a three-year interval results in significant CRC incidence reduction. The PLCO study[14] analyzed a subset of their cohort, concluding that surveillance resulted in a 30% reduction in CRC incidence, particularly in individuals with HRA. While these studies do not prove benefit, they provide some additional evidence which supports intensive surveillance for individuals with HRA.

CONCLUSIONS

New studies provide an evidence-based approach to colon polyp surveillance. There is now strong evidence that individuals with HRA at baseline colonoscopy have a risk of CRC after baseline colonoscopy which is 2 to 4 fold higher than individuals with LRA or no adenomas at a baseline screening exam. This supports the notion that biology is important – namely, that these individuals have whatever it takes in terms of genetic predisposition and lifestyle to develop CRC, and are most likely to benefit from surveillance. Current recommendations for a 3-year surveillance interval, would precede the development of CRC in most cases, and result in cancer prevention. Individuals with LRA have a risk of CRC similar to individuals with no adenomas. Surveillance benefit is uncertain, meaning that there is no evidence that surveillance will reduce CRC incidence or mortality in these individuals. New recommendations suggest a 7 to 10 year interval for surveillance, providing flexibility based on the quality of the baseline exam. Finally, there is new evidence that individuals with high-risk SSPs (≥1cm) do have a high risk of CRC and should have more intensive surveillance, similar to those individuals with HRA.

Colonoscopy quality impacts surveillance outcomes. The evidence that colonoscopy performed by endoscopists with low ADR is associated with higher risk of post-colonoscopy CRC highlights the importance of quality. The 2020 recommendations place quality as a cornerstone of the surveillance recommendations.[2] ■

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