Proximal Serrated Polyps Increase the Future Risk of Colorectal Cancer

Although it is widely accepted that patients with serrated polyps (SPs) have an increased risk of developing colorectal cancer (CRC), current guidelines are based on limited evidence regarding the magnitude of risk associated with large (≥1 cm) or small (<1 cm) SPs. However, the results of a large, retrospective cohort study published in Gastroenterology (published online February 7, 2020. doi:10.1053/j.gastro.2019.10.026) provides more precise information regarding these associations.

Study Details
The study was based on data from Kaiser Permanente’s Northern California district, which consists of approximately 4.3 million members from 21 medical centers. The members lived in suburban, urban, and rural areas and were considered to be “ethnically and socially diverse.” Researchers identified nearly 450,000 health plan members who received a colonoscopy and, after eliminating those with a prior history of polyps or CRC, known genetic syndromes, and other exclusion criteria, a total of 233,393 individuals were selected for the study population. Study patients were aged 50 to 85 years and had undergone their first colonoscopies between 2006 and 2016. Greater than one-half of the patients were at least aged 60 years. There were more females than males, with most of the patients reported as non-Hispanic white. All colonoscopies were performed either at ambulatory endoscopy centers or as inpatient procedures. Approximately one-third of the examinations were screening colonoscopies.

The patients’ SPs were categorized by size and location (proximal vs distal), but not by histological subtype. Because many of the colonoscopies were performed before the widespread use of current histological criteria for the diagnosis of sessile serrated lesions (SSLs), also known as sessile serrated adenomas or sessile serrated polyps, and because of high interobserver variation among pathologists for the subclassification of polyps with serrated features, the researchers used “SP” as a more general term to include hyperplastic polyps (HPs), traditional serrated adenomas, SSLs, or unspecified SPs. Although research indicates that the risk of CRC is higher for patients diagnosed with SSLs compared with those diagnosed with HPs, the 2 entities sometimes can be difficult to distinguish under a microscope, according to Dan Li, MD, a gastroenterologist at Kaiser Permanente Santa Clara Medical Center in Santa Clara, California, and researcher at the Kaiser Permanente Northern California Division of Research.

**KEY POINTS**

- Proximal SPs, particularly large ones, are associated with an increased risk of CRC.
- The results of this study support the USMSTF recommendation for follow-up colonoscopy at 3 years after diagnosis of a large (≥1 cm) SSL and at 5 to 10 years after diagnosis of a smaller SSL.
Hazard ratios and 95% confidence intervals (95% CIs) were calculated for CRC diagnosed 1 or more years after the patient’s colonoscopy based on polyp category versus no polyp. Cox proportional hazards models were adjusted for each patient’s age, sex, ethnicity, smoking history, and year the colonoscopy was performed.

Study Results

Of the study population of 233,393 patients, researchers found the following on their first colonoscopy:

- A total of 173,257 patients had no polyp identified.
- A total of 11,505 patients were classified with at least 1 proximal SP.
- A total of 12,080 patients were classified with at least 1 proximal SP and a synchronous adenoma.
- A total of 19,410 patients were classified with at least 1 distal SP.
- A total of 17,141 patients were classified with at least 1 distal SP and a synchronous adenoma.

Among patients with proximal SPs, a total of 1293 were classified as having a large SP and 9808 were classified as having a small SP. Patients with both large and small proximal SPs were placed in the “large SP” group. Distal SPs were not analyzed according to size because the number of patients with large distal SPs alone would have been too small to reach statistically reliable results.

The median follow-up from 1 year after colonoscopy was 3.6 years. Among the study population, there were 445 cases of incident CRC diagnosed more than 1 year after colonoscopy.

The cumulative incidence rates of CRC per 1000 individuals by SP subgroups at 5 years and 10 years after colonoscopy were:

- No polyp: 1.2 (95% CI, 1.0-1.4) at 5 years and 4.7 (95% CI, 4.0-5.6) at 10 years.
- Proximal small SP: 2.5 (95% CI, 1.4-4.3) at 5 years and 14.8 (95% CI, 9.0-24.3) at 10 years.
- Proximal large SP: 6.2 (95% CI, 2.3-17.0) at 5 years and 30.2 (95% CI, 13.2-68.4) at 10 years.
- Distal SP: 1.7 (95% CI, 1.1-2.6) at 5 years and 5.9 (95% CI, 3.6-9.5) at 10 years.
- Proximal SP with synchronous adenoma: 4.2 (95% CI, 2.9-6.3) at 5 years and 26.0 (95% CI, 16.1-42.0) at 10 years.
- Distal SP with synchronous adenoma: 3.0 (95% CI, 2.0-4.5) at 5 years and 12.1 (95% CI, 6.2-23.5) at 10 years.

“Our findings in this study confirmed our hypothesis that proximal serrated polyps, particularly large ones, are associated with increased risk of colorectal cancer, and therefore warrant close surveillance,” says Dr. Li. “Also, our findings support the current USMSTF (United States Multi-Society Task Force) recommendations, including performing colonoscopy at 3 years for large sessile serrated polyps and at a less frequent interval for small sessile serrated polyps.”

Study Analysis

“I have nothing but good things to say about the study,” says Durado Brooks, MD, MPH, vice president of Cancer Control Science at the American Cancer Society in Atlanta, Georgia. “Kaiser has such a tremendous advantage in doing this kind of work, particularly around colorectal screening, because of their electronic health records for such a huge number of patients and their outcomes over time. It’s almost unparalleled. There are few systems that can do this kind of detailed work, frankly.”

“Our study setting has very little selection bias, which is a unique strength,” says Dr. Li. “In addition, we used the incidence of colorectal cancer as the primary outcome, while many prior studies used advanced neoplasia or high-risk adenoma as the primary outcome.”

Although the study had some limitations, Dr. Brooks notes that the study authors have addressed them openly.

One such limitation, says Dr. Li, was the inability to assess the risk of CRC related to the subgroups of serrated polyps, such as SSLs versus HPs. “This needs to be further investigated in the future,” he says. “Additionally, the risk among individuals with synchronous conventional adenomas and serrated polyps needs to be better characterized.”

According to Dr. Brooks, the study is a good reminder that these types of lesions can influence a patient’s risk of developing future CRCs, and therefore clinicians need to be very diligent in their search for them. “I think it is also a good reinforcement for pathologists and gastroenterologists to remind them to look very carefully and make sure that they’re calling these lesions out, so the patients get the right kind of follow-up,” he says.

Dr. Brooks believes the study has value for primary care physicians as well. “It’s to their benefit to see the pathology reports for their patients after their colonoscopies. Not just whether polyps were removed, but also what kind of lesions, how many, and where they were located, because all of these factors impact when that patient needs follow-up,” he says. “The last thing you want to do if a patient has a concerning lesion removed is toss that information into the pile for a 10-year follow-up. That may be way too late to prevent their cancer.”

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