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Yield of second surveillance colonoscopy to predict adenomas with high-risk characteristics

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ABSTRACT

Background and aims: The yield of surveillance colonoscopies for patients with a history of polyps is well established for first surveillance, but limited for second surveillance. The aim of this study was to evaluate the proportion of high-risk adenomas at second surveillance colonoscopy based on findings of previous colonoscopies.
Methods: This retrospective cohort study was conducted in a tertiary hospital and patients who had undergone three colonoscopies were included. Based on the findings at index colonoscopy, patients were categorized into three groups: high-risk adenoma ($n = 252$), low-risk adenoma ($n = 158$) or no-adenoma ($n = 318$). Findings of subsequent high-risk adenoma, low-risk adenoma and no adenoma at surveillance colonoscopies were documented in each group.
Results: Among patients with high-risk adenoma at index and first surveillance colonoscopies, significantly higher rates of high-risk findings were found at second surveillance, compared with patients who had low-risk or no-adenoma at index colonoscopy and high-risk adenoma at first surveillance colonoscopy (58%, 33% and 10%, respectively, $p < 0.001$).
Conclusions: Both index colonoscopy and first surveillance high-risk adenoma have an impact on incidence high-risk findings at second surveillance colonoscopy and these subjects need close surveillance.

1. Introduction

Colonoscopy is the most commonly used modality for colorectal cancer (CRC) screening in the world. Detection and removal of polyps during colonoscopy reduce both CRC incidence and mortality [1–3]. Patients with adenomatous lesions are at increased risk for developing CRC and current guidelines [4] define 2 major groups for surveillance colonoscopy, based on the number, size and histology of adenomatous polyps at the baseline colonoscopy: (1) low-risk adenoma (LRA), defined as 1–2 tubular adenomas <10 mm, and (2) high-risk adenoma (HRA), defined as advanced adenoma (villous histology, high-grade dysplasia or >10 mm) or 3 or more non-advanced adenomas (NAA). HRA necessitates a follow-up colonoscopy after 3-years, whereas a 5–10-year interval is recommended for surveillance for LRA patients. Those with no adenoma should undergo repeat examination at 10 years.

In contrast, little information is available to guide surveillance intervals after the first follow-up colonoscopy. Three cohort studies [5–7], published in 2009 demonstrated that the risk of advanced neoplasia on the second surveillance colonoscopy corresponds with the findings of both the index and first surveillance examinations and are higher whenever HRA is found in one of them. Despite the inconsistency of these trials in defining HRA and time-intervals between colonoscopies, and the protocols which did not reflect clinical practice, recent recommendations were published based on these data [8]. Thus, the interval for the second surveillance is determined by the findings at the first surveillance colonoscopy (HRA, LRA or no adenoma), except when HRA is found at the index colonoscopy and no adenoma (NA) at first surveillance, in which case there is insufficient evidence to make a recommendation.

In a recent paper whose primary aim was to quantify the yield of high-risk findings on the second surveillance colonoscopy [9], Morelli et al. showed that when an adenoma (whether advanced or non-advanced) was present on the first surveillance colonoscopy, the index finding added no information (relative risk [RR] = 1.15) or only modest information (RR = 1.64), respectively, to high-risk

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findings at the second surveillance colonoscopy. However, surveillance intervals were shorter than the recommended 3- and 5-year intervals, and the population was homogenous, with no symptomatic indications for colonoscopy, which might not fully reflect a "real-life" setting.

In light of the limited published data regarding the true risk of HRA findings in 2nd surveillance colonoscopy with reference to findings in previous colonoscopies, the aim of this study was to assess the incidence of HRA (including colon cancer, advanced adenoma and ≥3 NAAs) at second surveillance colonoscopy based on the findings from index and first surveillance colonoscopies, in a more heterogeneous "real-life" symptomatic population, with time intervals determined by current recommendations for screening and by clinical practice.

2. Patients and methods

This retrospective cohort study was conducted at Meir Medical Center, Kfar Saba, Israel and affiliated gastroenterology clinics in the surrounding district, which serves a population of about 1 million. The study was approved by the institutional Ethics Committee. Data were collected from medical records from 1995 through 2013. Inclusion criteria for this study were all adult patients above 30 years of age who had a documented history of at least 3 colonoscopies – an index colonoscopy performed in the hospital and two surveillance examinations that could have been performed in the affiliated institutes, with colonoscopy and pathology reports available for evaluation. The interval between the procedures was at least 1 year and less than 10 years. Cases in which the indication for index or surveillance colonoscopy was other than screening (e.g. iron deficiency anaemia, rectal bleeding or abdominal pain), were included.

Patients were excluded if they had colorectal cancer that necessitated surgery as an indication for surveillance (including malignant polyps that were not endoscopically resected), personal history of inflammatory bowel disease or personal or family history of hereditary non-polyposis colon cancer (HNPCC), familial adenomatous polyposis (FAP), attenuated FAP and *muyth*-associated polyposis. Patients were also excluded if they had poor bowel preparation determined by the endoscopist, or incomplete examinations.

All data were abstracted from the medical records and included demographic information (gender, origin – Jews/Arabs); family history of colon cancer in first-degree relatives; number, size and histology of polyps found on the index and surveillance colonoscopies; either proximal or distal location of polyps, defined as distal to the splenic flexure; and interval between procedures. When more than one polyp was found, the most advanced (either in size or histology) was recorded for the purpose of categorization. Based on the findings at the index colonoscopy, the study population was categorized into 3 groups: (1) high-risk adenoma (HRA), which encompassed cases of advanced adenoma, including intra-mucosal carcinoma, or 3 or more non-advanced adenomas; (2) low-risk adenoma (LRA), which included 1–2 non-advanced adenomas; or (3) no adenoma (NA). Findings of HRA, LRA and NA from surveillance colonoscopies were documented in each group. The primary outcome was the rate of HRA in 2nd-surveillance colonoscopy in each of the study groups. In addition, we further sub-categorized the HRA study-group (at index colonoscopy) to patients with one vs. several characteristics of HRA findings (e.g. the presence of tubulovillous adenoma >10 mm).

2.1. Colonoscopy procedure

Bowel preparation included one of the three liquid preparation solutions (polyethylene glycol [PEG], sodium phosphate or sodium pico-sulfate), oral laxatives and enemas. The cleansing level was graded based on a validated 4-level scale. Patients with excellent, good or fair cleansing levels were defined as adequate preparation and included in the cohort, while those with poor cleansing level were not included.

The colonoscopy was performed under conscious sedation, with a combination of midazolam, fentanyl and propofol. During the procedure, standard endoscopic techniques were used for cleansing, detection and resection of polyps, including the use of white light, full cecal intubation and withdrawal time of at least 6 min. The size of the polyps was measured by the performing endoscopist and verified by the pathology report. According to our policy, all seen polyps, regardless of size or place, were resected during the procedure and sent to pathology.

Our recommendations for patients regarding interval-time after index colonoscopy were align with the accepted guidelines [4], i.e. 3 years for HRA or ≥3 NAAs, 5 years for 1–2 NAAs and 10 years when no adenoma was detected. The rate of adenoma-detection rate in screening colonoscopy was confirmed to be 25% in our institute between 2005 and 2013.

2.2. Statistical analysis

The chi-square test was applied for comparison of proportions between the different groups and within each group, in order to compare proportions with and without male gender and family history of colon cancer. Intervals were compared between risk groups using two-sample *t*-test. *p*-Value <0.05 was considered statistically significant. SPSS-21 software was used for statistical analysis.

3. Results

A total of 1529 patients underwent at least 3 colonoscopies within the study period, and after excluding patients with inflammatory bowel disease, colorectal cancer, genetic syndromes and poor preparation (Fig. 1), 759 patients who fulfilled the inclusion criteria were included in the cohort. After close review, 31 had incomplete or inconsistent data, including colonoscopy findings (20 patients), report on cleansing level (7 patients) or pathology report (4 patients), leaving 728 patients who were included in the final sample. At baseline, 318 patients had normal colonoscopy, 158 had LRA and 252 had HRA findings. Of the HRA group, 218 (86.5%) had advanced adenoma, 19 (7.5%) had intra-mucosal carcinoma (IMC) and 70 (27%) had ≥3 NAAs. Among the study population, 51% were male, 99.1% was Jews and only 0.9% were Arabs. The characteristics of the patients in each group at index colonoscopy are displayed in Table 1. The NA group was comprised of significantly more females and patients with family history of colon cancer than the other groups ($p < 0.001$). The quality of bowel cleansing in the study population was marked as good to excellent in 72%, while 28% had fair bowel preparation.

The results from patients with HRA, LRA or NA detection at the index colonoscopy are displayed in Table 2. The mean interval from index to first surveillance colonoscopy was 2.6, 4.1 and 5.3 years among HRA-, LRA- and NA groups, respectively ($p < 0.001$), as expected according to the recommendations. Among patients with HRA at index colonoscopy, 77 (31%) had high-risk findings at first surveillance colonoscopy, a significantly higher rate than patients with LRA (13% high-risk findings on first surveillance colonoscopy) or NA (9%), ($p < 0.001$). None of the patients with first surveillance HRA at had cancer.

Among patients with HRA at index colonoscopy, the frequency of high-risk findings on second surveillance colonoscopy was, as expected, related to the findings at the first surveillance colonoscopy. A higher rate of second surveillance HRA was found