Research

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Prediction of Outcomes in Colonoscopic Surveillance Among High-Risk Individuals

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1. Abstract

1.1. Objective: Colonoscopy surveillance in individuals who have a higher risk of developing colorectal cancer must rely on appropriate patient selection and optimal screening intervals. This study aimed to identify factors that predict the presence of neoplastic lesions during colonoscopy in individuals with a familial risk of colorectal cancer.

1.2. Design: A total of 1,203 participants with at least a twofold increased risk of colorectal cancer due to family history were included in a long-term colonoscopy surveillance program. Logistic regression analysis was used to evaluate the influence of family-related risk variables on the presence of adenomas and advanced adenomas. Additionally, findings from the initial colonoscopy were analyzed to determine their association with lesions detected during subsequent surveillance.

1.3. Results: After adjusting for age, the occurrence of advanced lesions was significantly related to the number of first-degree relatives diagnosed with colorectal cancer and to early disease onset (before 50 years) in the youngest affected family member. No significant relationship with gender was observed. Family history had only a minor effect on the occurrence of simple adenomas. Future advanced lesions were mainly predicted by the presence of advanced lesions at the baseline colonoscopy. In contrast, the risk of detecting new adenomas was associated with the presence of adenomas, advanced lesions, and hyperplastic polyps during the first examination.

1.4. Conclusion: Risk factors for simple adenomas and advanced lesions appear to differ. The most significant predictors of advanced lesions were a higher number of first-degree relatives with colorectal cancer and early onset of the disease within the family. Findings of small adenomas or hyperplastic polyps did not significantly predict the development of advanced lesions during follow-up.

2. Keywords: Colorectal cancer, colonoscopy, surveillance, family history, risk assessment

3. Introduction

Colorectal cancer (CRC) is among the most frequently diagnosed cancers worldwide and is a major cause of cancer-related mortality. Approximately one-quarter of CRC cases occur in individuals who report a family history of the disease. However, inherited single-gene disorders account for fewer than five percent of all cases. The most common hereditary conditions associated with CRC include Lynch syndrome, caused by mutations in mismatch repair genes, and familial adenomatous polyposis, which results from mutations in the APC gene.

Apart from these inherited syndromes, the most important risk factors for CRC include increasing age and the presence of affected first-degree relatives. Individuals with multiple first-degree relatives diagnosed with CRC may experience a two- to eightfold increase in risk compared with those without such a history.

In most instances, colorectal cancers develop from precursor lesions known as adenomas. These lesions can gradually progress to malignancy, and in some hereditary conditions such as Lynch syndrome this transformation may occur more rapidly. Colonoscopy plays a critical role in preventing CRC because premalignant lesions can be detected and removed during the procedure, reducing both incidence and mortality.

Although colonoscopy is an effective screening method, it is also resource-intensive. Therefore, identifying individuals who will benefit most from surveillance and determining the optimal timing for screening are essential. In moderate-risk populations with a family history of CRC, it may be possible to identify subgroups with particularly high risk and prioritize them for colonoscopic surveillance.

Several factors related to family history may influence CRC risk. These include the number of first-degree relatives affected, the presence of second- or third-degree relatives with CRC, the type of relationship with the affected family member, and the age at which the disease first appeared in the family. The presence and characteristics of colorectal polyps, particularly adenomas, may also indicate an increased risk for future cancer development. For this reason, polyp characteristics such as number, size, and histological type are often evaluated during surveillance programs. This study examines data from a 20-year colonoscopy surveillance program involving individuals with an elevated familial risk of

INSIGHT JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY

colorectal cancer. The aim was to determine which clinical and familial factors predict the development of adenomas and advanced lesions during follow-up.

4. Methods

4.1. Study Population

Since 1990, individuals with an estimated twofold or higher risk of colorectal cancer due to family history have been offered genetic counseling and surveillance through the Clinical Genetics Department at Karolinska University Hospital in Stockholm, Sweden. Data collected between January 1990 and June 2010 were analyzed for this study.

Participants were eligible if they had at least two relatives with colorectal cancer among first-, second-, or third-degree relatives, or if a first-degree relative had been diagnosed with CRC before the age of 50. Individuals diagnosed with hereditary syndromes such as familial adenomatous polyposis or Lynch syndrome were excluded through established clinical diagnostic procedures including genetic and molecular testing.

Participants underwent screening colonoscopy approximately every three years. Individuals who had already been diagnosed with colorectal cancer before entering the program were excluded. All data used in the analysis were anonymized, and ethical approval was obtained from the regional ethics committee in Stockholm.

4.2. Colonoscopy Procedure

Most colonoscopies were performed at Karolinska University Hospital, although some examinations were conducted at other facilities and reported to the study center. Standard video colonoscopy equipment was used. The quality of procedures met European guidelines for colorectal cancer screening, including standards for bowel preparation, completeness of examination, and adenoma detection rates.

During each procedure, all polyps were documented with regard to location, size, and appearance. Polyps were removed whenever possible using standard endoscopic techniques and were sent for histopathological evaluation.

Lesions located at or above the splenic flexure were classified as right-sided, while those located distally were considered left-sided. Adenomas were categorized based on World Health Organization criteria into tubular, tubulovillous, villous, or serrated types. Dysplasia was graded as either low-grade or high-grade.

Advanced lesions were defined as colorectal cancer or adenomas larger than 10 mm, adenomas containing more than 20% villous components, or lesions displaying high-grade dysplasia.

The surveillance period was calculated from the first colonoscopy to the last recorded examination. Detailed family pedigrees were created for each participant, documenting affected relatives and the youngest age at diagnosis within the family.

4.3. Statistical Analysis

Statistical analyses were performed using Statistical software (version 10.0). Differences in mean age between subgroups were evaluated using Student's t-test. The occurrence of adenomas and advanced lesions during surveillance was analyzed using chi-square tests. Multivariate logistic regression models were used to evaluate the influence of variables such as age, sex, duration of follow-up, and baseline findings (hyperplastic polyps, adenomas, or advanced lesions).

The expected number of colorectal cancer cases in the cohort was estimated using age- and sex-specific incidence rates from the Swedish population.

5. Results

5.1. Participant Characteristics

The study included 1,203 individuals from 521 families. Of these participants, 470 (39%) were men and 733 (61%) were women. A total of 676 participants had one first-degree relative with colorectal cancer, while 299 had two or more affected first-degree relatives. The remaining 228 individuals had only second- or third-degree relatives with the disease.

Nearly half of the participants had at least one first-degree relative diagnosed before the age of 50. The average age at the first colonoscopy was approximately 52 years.

A total of 2,293 colonoscopy examinations were performed. About half of the participants underwent more than one examination during the study period. The average follow-up time among individuals participating in surveillance was about 55 months.

5.2. Colonoscopy Findings

Six colorectal cancer cases were identified in five individuals. Four cancers were detected during the initial screening colonoscopy, while two were found during surveillance. The observed number of screening cancers was significantly higher than the expected number based on general population data.

Advanced lesions were more frequently detected in individuals with multiple first-degree relatives affected by colorectal cancer and in those whose relatives developed the disease at an early age. However, the occurrence of simple adenomas showed weaker associations with family history.

6. Discussion

Colonoscopy surveillance is widely recommended for individuals with a family history of colorectal cancer. Nevertheless, guidelines differ regarding the appropriate starting age and interval between examinations. The primary objective of this study was to determine which familial and clinical factors most strongly predict the

INSIGHT JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY

development of advanced lesions during surveillance.

The findings suggest that the number of first-degree relatives affected by colorectal cancer significantly influences the risk of advanced lesions. In contrast, this relationship was less pronounced for simple adenomas. These observations are consistent with previous research indicating that family history is an important risk factor for colorectal cancer but may not strongly predict the development of small adenomas.

Another key observation was that early onset of colorectal cancer within the family increased the likelihood of detecting advanced lesions in participants. This supports the concept that early familial disease may indicate a stronger genetic predisposition.

The study also examined whether findings at the baseline colonoscopy could predict future lesions. Advanced lesions detected at the initial examination were strongly associated with the occurrence of advanced lesions during follow-up. In contrast, small adenomas or hyperplastic polyps did not appear to predict future advanced disease.

One limitation of the study was that only about half of the participants underwent repeated surveillance examinations, and the average follow-up period was relatively short. This was partly due to the large number of participants recruited toward the end of the study period.

Overall, the results indicate that different biological mechanisms may underlie the development of simple adenomas and advanced lesions. For surveillance programs, particular attention should be given to individuals with multiple affected first-degree relatives, early onset of colorectal cancer within the family, and advanced lesions detected during baseline colonoscopy.

These findings may help improve the design of colonoscopy surveillance strategies for individuals with familial risk of colorectal cancer.

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