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Low Prevalence of Criteria for Early Screening in Young-Onset Colorectal Cancer

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Introduction

Colorectal cancer (CRC) incidence in adults aged <50 years is increasing in the U.S. despite an overall decline in CRC incidence in the general population.[1,2] This trend has received attention in the general and medical press.[3] The underlying factors for this trend are unknown.[4]

Current guidelines recommend CRC screening in people aged <50 years with specific patterns of family history of CRC, such as a first-degree relative with CRC or advanced adenoma diagnosed when aged <60 years, in people with longstanding inflammatory bowel disease, and in those with cancer genetic syndromes. Few studies have examined the proportion of patients diagnosed with young-onset (aged <50 years) CRC who bear these risk factors.

It has been estimated that approximately 23% of patients with young-onset CRC have a family history of CRC.[5] Recently, a study of universal cancer gene panel testing found that 16% of patients with CRC at age <50 years have a mutation in a cancer predisposition gene.[6]

Recently, a cohort of patients with young-onset CRC at a large academic center was described, focusing on times to diagnosis and the relationship with cancer stage.[7] This study's aims are to determine the fractions of young-onset CRC patients in the same cohort who had recognized risk factors for early CRC, as a function of age by decade. It is hypothesized that only a minority at all ages would qualify for early screening based on existing recommendations.

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Methods

This study was approved by the Stanford IRB and identified 253 patients with a diagnosis of colorectal adenocarcinoma who were seen at the Stanford Cancer Institute between 2008 and 2014. Hereditary cancer syndromes were defined as Familial Adenomatous Polyposis, Lynch Syndrome, MYH-associated Polyposis, and Li–Fraumeni Syndrome. Patients with suspected hereditary cancer syndromes based on abnormal tumor immunohistochemistry were classified as confirmed, probable, possible, or Lynch syndrome excluded upon a detailed review. Family history of CRC was defined as the presence of a first-degree relative, second-degree relative, or third-degree relative with CRC. All data were abstracted by chart review and maintained in a REDCap (https://redcap.stanford.edu) database. Analyses were performed in SAS, version 9.4 in 2017.

Results

The prevalence of a family history of CRC ranged from 39% in individuals aged 20–29 years to 23% in the group aged 40–49 years, but only 13% and 6%, respectively, had a first-degree relative with CRC (Table 1). A hereditary cancer syndrome was confirmed in 13% of individuals aged 20–29 years, 5.2% of the group aged 30–39 years, and 2.9% of the group aged 40–49 years. But only one patient, a male aged 26 years with familial polyposis, had been diagnosed with a hereditary cancer syndrome prior to CRC diagnosis; all other patients were the proband for genetic testing for their family. Only 8.7% of individuals aged 20–29 years and 1.7%–1.8% of the group aged 30–49 years carried a diagnosis of inflammatory bowel disease. The majority of patients in each age stratum (70% of the entire cohort) met none of the classic indications for early CRC screening (Table 1).

Discussion

Only a minority of patients in this cohort with young-onset CRC had the recognized risk factors of a family history of CRC, personal history of inflammatory bowel disease, or a hereditary cancer syndrome. These risk factors were more common at younger ages. In most cases of hereditary cancer syndromes, the young patient was the proband for the family.

Recently, Pearlman et al.[6] reported inherited cancer gene mutations associated with CRC in four of 18 (22%) individuals aged 20–29 years, 19 of 98 (19%) individuals aged 30–39 years, and 36 of 333 (11%) individuals aged 40–49 years undergoing cancer gene panel testing after CRC diagnosis. The respective rates of confirmed hereditary syndromes in this letter (13%, 5.2%, 2.9%) suggest that comprehensive, universal gene panel testing[6] identifies substantially more affected patients than does routine care.

The authors acknowledge this single-institution study's limitations, including potential lack of generalizability and small sample size.

These findings suggest that even optimal adherence to existing screening guidelines would likely exclude from early screening the majority of patients aged <50 years who develop CRC. Expanded cancer gene panel testing in young persons diagnosed with CRC today might identify relatives at risk in whom young-onset CRC might be prevented in the future.

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Further exploration of potential clinical risk factors or biomarkers that might select younger persons for early screening is warranted.

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Table 1

Young-onset CRC by Age Group and Risk Factors

Risk factors	Age <20 years (*n*=1)	Age 20–29 years (*n*=23)	Age 30–39 years (*n*=58)	Age 40–49 years (*n*=171)	Total age <50 years (*n*=253)
Any family history of CRC	0	9 (39.1)	14 (24.1)	40 (23.4)	63 (24.9)
≥1 FDR with CRC	0	3 (13.0)	4 (6.9)	10 (5.9)	17 (6.7)
Had confirmed hereditary cancer syndromes	0	3 (13.0)	3 (5.2)	5 (2.9)	11 (4.4)
Had confirmed, probable, or suspected hereditary cancer syndrome	0	4 (17.4)	5 (8.6)	9 (5.3)	18 (7.1)
Had inflammatory bowel disease	0	2 (8.7)	1 (1.7)	3 (1.8)	6 (2.4)
No family history of CRC, hereditary cancer syndrome, or inflammatory bowel disease	1 (100)	12 (52.2)	39 (67.2)	125 (73.1)	177 (70.0)

Note: Data are presented as *n* (%). Percents are based on n in each age group.

CRC, colorectal cancer; FDR, first-degree relative.

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