What about the guys? An assessment of gender differences in hereditary colorectal cancer testing

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Background

Approximately 5-10% of colorectal cancer (CRC) is due to hereditary causes. Identification of an inherited cause may impact surgical and treatment decisions for CRC patients and may identify increased risks for other cancers that warrant increased screening and/or risk reduction measures. Men have testing for hereditary breast and ovarian cancer less often than women, even though these genes may also cause increased risk for cancer in men and men are as likely as women to carry mutations in these genes and pass them onto their children. We aimed to explore whether similar gender differences exist related to testing for hereditary CRC.

Methods

We retrospectively reviewed clinical data and test results from consecutive CRC cases, who had a multi-gene panel with 13-49 genes at our laboratory, between March 2012 and June 2016. Statistical comparisons between males and females were conducted using Fisher's exact test.

Results

Of CRC cases (n=7142), 61.1% were female and 12.8% were positive for mutation or likely pathogenic variant. Average age of CRC onset for men was 47.2, and for women was 49.5. Women with CRC before age 20 had the highest mutation rate (31.8%), but men were more likely to test positive than women overall (14.1% vs 12.0%, p=1.1e-2). Mutations were most frequent in the same three genes for both men and women, but in different orders: *MLH1, CHEK2,* and *MSH2* for males and *CHEK2, MSH2,* and *MLH1* for females. The only genes with significant differences in mutation rates between men and women were *MLH1* (3.2% vs 1.5%, p=2.0e-6) and *MSH6* (1.7% vs 0.8%, p=3.0e-3).

Conclusions

Hereditary CRC is expected to affect men and women equally. In our cohort, however, the majority of individuals tested were women, while men were more likely to test positive. Possible explanations include smaller sample size and earlier age of onset in men, perceptions of referring clinicians, and different levels of interest in genetic counseling and testing between male and female patients. These data highlight an important opportunity for educating and identifying more men with hereditary CRC who may benefit from genetic information. Further studies are needed to confirm these results and explore reasons for the differences.