Re: Risks of Colorectal and Other Cancers After Endometrial Cancer for Women With Lynch Syndrome

In a recent article in the Journal, Win and colleagues (1) demonstrated that the risk of colorectal cancer after endometrial cancer is statistically significantly increased in women with Lynch syndrome. The authors also reported a higher risk of kidney, renal pelvic, ureter, urinary bladder, and breast cancer in these patients. Although the results of their study expand our understanding of Lynch syndrome, we would like to note some additional factors that warrant discussion.

First, obesity is a risk factor for colorectal cancer (2). Higher endometrial cancer incidence rates in the obese population have also been reported (3). Patients included in this study with a history of endometrial cancer might have also been obese, which would have substantially increased their risk of colorectal cancer. Another recent study revealed a higher risk of colorectal cancer in women with a history of endometrial cancer but not Lynch syndrome (4). Therefore, obesity might have independently affected the results of the study by Win and colleagues. Moreover, the dietary habits that increase the risk of endometrial cancer also increase the risk of colorectal cancer (5, 6). However, the impact of diet on patient outcomes was not assessed in this study.

Finally, the authors reported an increased risk of the aforementioned cancers compared with the risk in the general population. However, we don’t know whether the risk of those cancers in patients with a history of endometrial cancer and Lynch syndrome is also higher than the risk in patients with Lynch syndrome but no history of endometrial cancer.

Overall, to understand the risk of colorectal cancer in women with previous endometrial cancer and Lynch syndrome, further prospective studies controlling for epidemiologic risk factors are warranted.

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Note
All authors contributed equally. The authors declare no conflicts of interest.

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Response
Oktay et al. raise two issues related to our recent study on risks of colorectal and other cancers after endometrial cancer for women with Lynch syndrome (1). Oktay et al. suggest that obesity and/or diet might have independently contributed to the increased risk of colorectal cancer we observed, given they are risk factors for endometrial and colorectal cancer for women in the general population (i.e., they are potential confounders). We argue that these lifestyle factors are unlikely to have an impact on our estimation of cancer risks. First, one of our measures of association was a comparison between incidences of cancers after endometrial cancer for women with Lynch syndrome and incidences of cancers after endometrial cancer for women from the general population [see Table 3; SIR, for colorectal cancer = 36.3, 95% confidence interval = 25.8 to 49.6 (1)]. For this comparison, the only difference between the two groups of women was whether the women carried a germline mutation in a mismatch repair gene, which is not associated with body mass index or diet, and therefore this measure of association cannot be due to confounding with obesity or diet. Second, in contrast with women from the general population, we have reported in a previous study that obesity is not associated with an increased risk of endometrial cancer for women with Lynch syndrome (2).

Third, in our study of women with Lynch syndrome and history of endometrial cancer, there was no difference in body mass index at age 20 years between those who did and did not develop colorectal cancer (mean = 22, standard deviation [SD] = 3.7 vs mean = 22, SD = 4.0 kg/m²; P = .61). Similarly there was no difference in recent body mass index (within 2 years before interview) between those who did and did not develop colorectal cancer (mean = 27, SD = 6.0 vs mean = 27, SD = 5.9 kg/m²; P = .51). There was also no evidence of difference in intakes of fruit, vegetables, and red meat between those with and without colorectal cancer (data not shown).

Oktay et al. also claim, “[W]e don’t know whether the risk of those cancers in patients with a history of endometrial cancer and Lynch syndrome is also higher than the risk in patients with Lynch syndrome but no history of endometrial cancer.” In fact, we have examined and reported on this by comparing cancer risks for women who had Lynch syndrome and history of endometrial cancer with cancer risks for women who had Lynch syndrome but no prior history of any cancer (3) [See detail