The Oversimplification of Uterine Cancer Classifications and Risk Factors.

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In reply to comments on “The Association of Obesity and Type I Uterine Cancer - Is This an Oversimplification?”. First, we appreciate Dr. Sarkar et al for their interest in our study and thoughtful comments. We agree with their comment that a direct analysis evaluating obesity in those presenting with non-endometrioid tumors is important. However, this would require a prospective, longitudinal cohort study over many years to accomplish. Our analysis was one of the first studies to utilize population-level data over two decades to evaluate the association of obesity and the rising rate of high-risk, non-endometrioid tumors. One of the significant weaknesses of our study involves the use of two national databases that limits our ability to perform a direct correlation due to the lack of patient-level data. When patient-level data was available in smaller epidemiologic studies, evidence does suggest overlapping risk factors between both type I and type II endometrial cancer, including obesity.\(^1\) Thus, our findings add to the growing body of literature that suggests that obesity may play a role in high-risk, non-endometrioid tumors.

Given the rising incidence and mortality of endometrial cancer, we hope these findings will direct future research to explore the impact of obesity on the incidence of non-endometrioid tumors. Ideally, as Dr. Sakar et al noted, such a study would include an analysis of body mass index and its association with types of endometrial cancer according to the molecular classification suggested by the Cancer Genome Atlas.\(^2\) It would also ideally include a longitudinal, international analysis evaluating the impact of all other known and potentially unknown risk factors such as demographic, socioeconomic, environmental, dietary, physical activity, family, hormonal, menstrual, parity, genetic, proteomic, metabolomic, epigenetic, and microbiomic factors. Clearly, the role of obesity on type II tumors, as well as the entirety of the traditional type I/II classification system may be oversimplified in light of the molecular classification of endometrial cancer.\(^3\) Future studies should aim to validate a molecular classification system and determine associated modifiable risk factors in order to abate the rising incidence and mortality associated with endometrial cancer.
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References

