The association of obesity and type I uterine cancer: is this an oversimplification? A comment

TO THE EDITORS: The study titled “The association of obesity and type I uterine cancer—is this an oversimplification?” by Eakin et al1 has been instrumental in raising a pursuit for analyzing the potential effect of obesity on the rising trend of type II endometrial cancer during the recent years. The classical teaching on obesity as a major risk factor for type I endometrial cancer is now being debated.1,2 We appreciate the authors for conducting this large-scale multicentric cohort study for a substantial period of 17 years. However, we wish to clarify certain observations that will further help in better comprehending the results.

Foremost, it would have been better if the analysis was performed as to whether the patients presenting with type II endometrial cancer being recruited in the study had a body mass index (BMI) of $>30$ kg/m$^2$. A correlation of BMI with the molecular classification of cancer will help to establish the hypothesis of the study. Moreover, a detailed analysis of other antecedent factors leading to endometrial cancer, such as familial history, nulliparity, assisted reproductive techniques, and exogenous hormonal therapy, needs to be evaluated in detail. These confounding factors need to be addressed before justifying our observations. Furthermore, certain modifiable risk factors for type I endometrial cancer might have been addressed by the changing lifestyles in recent years. In contrast, type II cancers are usually attributable to genetic non-modifiable risk factors.3 Therefore, further exploration into this aspect can help to uncover newer facts about the root cause of both types I and II endometrial cancers. This study will ultimately help in addressing the oncology team to delve into the matter and will probably stimulate researchers worldwide to provide a better classification of endometrial cancer.

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REFERENCES

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The oversimplification of uterine cancer classifications and risk factors

We appreciate Dr Sarkar and colleagues for their interest and thoughtful comments on our study titled “The association of obesity and type I uterine cancer-is this an oversimplification?.” We agree with their comment that a direct analysis evaluating obesity in those presenting with nonendometrioid tumors is important. However, this would require a prospective, longitudinal cohort study over many years to accomplish. Our analysis focused on the use of population-level data over 2 decades to evaluate the association between obesity and the rising rate of high-risk, nonendometrioid tumors. Of note, one of the significant weaknesses of our study involved the use of 2 national databases that limited our ability to perform a direct correlation because of the lack of patient-level data. When patient-level data were available in smaller epidemiologic studies, evidence suggested overlapping risk factors between types I and II endometrial cancers, including obesity.1 Thus, our findings have added to the growing body of literature that suggests that obesity may play a role in high-risk, nonendometrioid tumors.

Given the rising incidence and mortality of endometrial cancer, we hope these findings will direct future research to explore the effect of obesity on the incidence of nonendometrioid tumors. Ideally, as Dr Sakar and colleagues noted, such a study would include an analysis of body mass index and its association with the types of endometrial cancer according to the molecular classification suggested by the Cancer Genome Atlas.2 Furthermore, it would ideally include a longitudinal, international analysis evaluating the effect 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. The role of obesity on type II tumors and the entirety of the traditional type I or II classification system may be