Letter to the Editor

Unbalanced Cancer Status May Undermine Results on Insulin and Insulin-like Growth Factor

To the Editor: Irwin et al. (1) found that an exercise intervention reduced levels of insulin-like growth factor (IGF) and insulin among postmenopausal breast cancer survivors. However, we are concerned that the authors’ randomization failed to evenly distribute lower- and higher-grade cancers. Particularly, a significantly larger number of participants with higher-grade breast cancer were located in the control group than in the intervention group.

The authors note that the two study groups did not differ on any baseline criteria at a statistically significant level. We tested this statement with regard to cancer grade in two ways using the data provided in the article. First, we performed a Wilcoxon rank sum, which yielded a $P$ value of 0.0505. Second, we combined some of the cancer stages into larger categories to better power the analysis of this relatively small study ($n = 75$). We combined in situ carcinoma and stage I and compared that group to the combination of stage II and IIIa as the authors did in the stratified analysis. The result of the $\chi^2$ test of those two groups was a $P$ value of 0.016.

The larger number of more severe cancers among the usual care group could confound or modify the results. Later-stage cancer is a risk factor for increased cancer recurrence and death. If IGF or insulin is associated with cancer progression, the higher levels found among the usual care group may simply be an indicator of their more serious cancers. This notion is supported anecdotally by the higher levels of insulin and IGF found at baseline in the usual care group and by the increase in both insulin and IGF that the usual care group experienced over the course of the study. Many other potential mechanisms could be at play here. We posit only one to show the nature of our concern about the unbalanced cancer status of study participants.

We are optimistic that exercise can yield positive changes both in the rate of cancer recurrence and in the levels of cancer risk factors. We also understand that randomization cannot reliably distribute baseline characteristics evenly when samples are small. However, we are concerned that the uneven distribution of risk factors may be responsible for the results found by the authors. The authors should either adjust for breast cancer stage in the analysis or conclude their findings based on the stratified analysis. We believe that the issue at least merited discussion, and are concerned that it received none.

Asher Wolf
Ka He
Pengcheng Xun
Elizabeth R. Hoffman
James A. Smith
Elizabeth M. Widen
Department of Nutrition at the
UNC Gillings School of Public Health,
Chapel Hill, North Carolina

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References
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Asher Wolf, Ka He, Pengcheng Xun, et al.


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