Re: “Sex-Specific Prognostic Significance of Obesity in Nonmetastatic Clear-Cell Renal-Cell Carcinoma in Korea: A Large Multicenter Cohort Analysis”: Fallacious statistical inference led to an unsupported conclusion.

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To the Editor,

We read with interest the recent paper of Byun and colleagues (1), which reported an analysis of obesity in relation to prognosis of clear cell renal cell carcinoma (RCC). Their analysis of over 2000 patients with non-metastatic RCC suggested that BMI is inversely associated with risk of both recurrence and RCC cause-specific death. This observation, along with prior studies of obesity and RCC prognosis (2–5), provides considerable support for the existence of an “obesity paradox” in RCC, whereby obesity is associated with higher risk of RCC, but is paradoxically indicative of better prognosis.

Byun and colleagues further performed an analysis stratified by sex, which led them to conclude that obesity was a favourable prognosticator in male but not female patients. This conclusion is based on invalid statistical inference, and indeed no relevant evidence is presented to support the assertion that BMI is prognostic for men but not women. Their conclusion rests on a comparison of statistically “significant” and “non-significant” point estimates. This difference between “significant” and “non-significant” is not itself necessarily statistically significant (6). In this case the estimated hazard ratios (HR) are remarkably similar for men and women, and it is unlikely that there is compelling statistical evidence that the association between BMI and risk of death or recurrence differs by sex. For example, Byun et al report that the HR for cause-specific mortality for an unspecified continuous increment in BMI was 0.82 (95% CI [0.75, 0.90]) for men, and 0.90 [0.78, 1.05] for women. Despite the fact that the association was not statistically significant among women, the estimates are clearly compatible with a lower rate of death for those with higher BMI, regardless of sex. Similarly when comparing high (≥ 25 kg/m²) versus normal (18.5–25 kg/m²) BMI, the HR for cause-specific mortality was similar for men (0.58 [0.35, 0.95]) and women (0.63 [0.25, 1.56]). P-value functions for these estimates are plotted in Figure 1, which demonstrate the similarity of these estimates for men and women.

If the authors wished to make the case for a difference in the magnitude or presence of association by sex, they could have presented results from a statistical test of the interaction between BMI and sex. Evaluating estimates as “significant” among men, and “non-significant” among women is insufficient (6). In the absence of such evidence, the main conclusion of their paper is unsupported. Indeed, it is unsurprising that HRs were estimated much more precisely for men than women, and were therefore more likely to surpass any given statistical significance threshold, as kidney cancer is twice as common among men compared with women (7). This is reflected in the sample of patients analysed by Byun et al., which consisted of 1524 men and only 573 women. The greater precision in their estimates for men compared with women is clearly displayed in Figure 1.

In summary, the conclusion that obesity is an indicator of good prognosis from RCC among men but not women is not supported by the analysis and results reported by Byun et al., and stems from the fallacious reasoning that “significant” and “non-significant” estimates must themselves differ importantly. The estimated HRs reported by Byun et al. are consistent with higher BMI at diagnosis being associated with better prognosis from RCC for both men and women.

Figure captions

Figure 1: P-value functions for men (yellow) and women (blue): (A) for continuous BMI, and (B) for BMI ≥ 25 versus 18.5–25 kg/m². The horizontal dashed line indicates P=0.05.

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