

Explaining the Obesity Paradox—Response Bette J. Caan<sup>1</sup>, Jeffrey A. Meyerhardt<sup>2</sup>, and Carla M. Prado<sup>3</sup>

We appreciate the letter of Winkels and colleagues (1) who, with two pertinent points, underscore the importance of providing data that will allow readers to compare our results with those from other studies. First, as noted in their letter, 17% of our patients had their CT scans after colorectal cancer surgery, which could affect their body composition. Even though all scans were taken before administration of chemotherapy, we agree that sensitivity analyses of only patients who had CT scans before surgery would provide the best estimate of at-diagnosis body composition. Our analyses of those patients ( $n = 2,701$ ) whose CT scan was administered before surgery found HRs for the effect of sarcopenia on both overall and colorectal cancer mortality were almost identical to those in the larger patient population reported in our original article (2). Including only presurgery CT scans, the HR for sarcopenia and overall mortality was HR = 1.21 [95% confidence interval (CI), 1.02–1.42] compared with HR = 1.27 (95% CI, 1.09–1.48) reported in our article, and for sarcopenia and colorectal cancer-specific mortality, the HR was 1.41 (95% CI, 1.14–1.75) compared with HR = 1.46

(95% CI, 1.19–1.79) reported in our article. Other results reported in Table 2 were similar as well.

Second, in response to Winkels and colleagues' question on our use of muscle as a variable, we chose to present skeletal muscle area at the L3 in tertiles, with simultaneous adjustment for body mass index (BMI), a measure of body size, as a demonstration that absolute muscle area is also an important predictor of survival. As requested, we reanalyzed the data in Table 2 and Fig. 3 using SMI (skeletal muscle index), substituting sarcopenia to define low muscle, instead of the lowest tertile of absolute muscle area. Again, results were almost identical. In Fig. 3, when sarcopenia was used to define low muscle instead of absolute muscle area, 57% of those with a BMI between 25 and 30 kg/m<sup>2</sup> were considered normal (neither high adiposity or low muscle) compared with 58.6% reported in our article. Similarly, in the phenotype analyses (Table 2), effects for low muscle, or low muscle and high adiposity, on overall mortality defined by sarcopenia were similar, even slightly stronger with HR = 1.42 (95% CI, 1.18–1.70) and HR = 1.49 (95% CI, 1.16–1.92) respectively, compared with HR = 1.33 (95% CI, 1.10–1.61) and HR = 1.40 (95% CI, 1.03–1.90) when low muscle was defined by absolute muscle area.

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**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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