editorials

Mounting Weight of Evidence on the Importance of Body Weight for Men With Prostate Cancer

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Obesity is a well-established public health problem in the United States, with approximately 40% of people in the country categorized as obese.[1] Obesity is set to overtake tobacco as the leading cause of preventable cancer in the United States.[2] Among men with prostate cancer, obesity has been associated with a higher risk of recurrence after localized disease, higher risk of developing metastatic disease, and higher risk of prostate cancer–specific mortality.[3] Observational evidence also suggests that even modest weight gain is associated with an increased risk of prostate cancer recurrence,[4,5] fatal prostate cancer,[6] and prostate cancer–specific mortality after a diagnosis of prostate cancer.[7]

Because observational studies of obesity and prostate cancer have focused on weight and weight change before or near the time of diagnosis, less is known about the impact of postdiagnostic obesity and/or postdiagnostic weight change on outcomes among these men. In the article accompanying this editorial, Troeschel et al[8] help to answer how body mass index (BMI) after a diagnosis of prostate cancer, along with subsequent weight change, affects prostate cancer–specific, cardiovascular, and all-cause mortality among a large, prospective cohort of men with nonmetastatic prostate cancer from the Cancer Prevention Study-II Nutrition Cohort.

Using data from 8,330 men, Troeschel et al[8] evaluated the association between postdiagnostic obesity and prostate cancer mortality. Although risk was nonsignificantly higher overall, there was a significant positive association between postdiagnostic obesity and prostate cancer mortality among men with low-risk tumors (defined as T1/T2 or Gleason $\leq$ 7 tumors). Among the 6,942 men with repeated weight measures, men who gained $>$ 5% of body weight after their prostate cancer diagnosis also had a higher risk of death resulting from prostate cancer when compared with men who maintained a stable weight, even after adjustment for baseline BMI. These are important observations, given men with nonmetastatic prostate cancer have been noted to have a long life expectancy.[9] This highlights the importance not only of obesity avoidance but also of weight maintenance. It also brings forth an obvious question: if obesity and weight gain are risk factors for death resulting from prostate cancer, is weight loss protective?

Across disciplines, clinicians recommend weight loss for overweight and obese patients, given the negative effect obesity has on many clinical outcomes. However, there is a paucity of evidence within prostate cancer as to whether weight loss improves cancer-specific outcomes. In this study, weight loss was not associated with prostate cancer mortality. However, the evaluation of self-reported weight loss, which could be a consequence of underlying illness, is not the same as an evaluation of the impact of intentional weight loss among men with prostate cancer. Indeed, in a review of the National Cancer Institute research portfolio of a decade of studies on physical activity and energy balance among cancer survivors, officials implored researchers to evaluate the impact of weight loss interventions among cancer survivors on outcomes relevant to survivors and clinicians.[10] Fortunately, accumulating evidence from completed and ongoing trials is now addressing the impact of weight loss on clinical outcomes among men with prostate cancer (ClinicalTrials.gov identifiers: NCT03261271 and NCT03971591) and across disease types, including, for example, men with low- to intermediate-risk disease (PALS trial; ClinicalTrials.gov identifier: NCT02454517) and men with biochemical recurrence (EMPOWER trial; ClinicalTrials.gov identifier: NCT04266431).[11]

Importantly, Troeschel et al[8] also evaluated the influence of obesity and weight change on cardiovascular disease (CVD) –related mortality. Although weight change was not associated with CVD mortality, postdiagnostic obesity was associated with a significantly higher risk of CVD-related mortality. Androgen-deprivation therapy, the primary treatment for advanced prostate cancer, has also been associated with an increased risk of cardiovascular risk factors and mortality in some studies.[12] In sensitivity analyses where these men were removed, obese men still had a significantly higher risk of cardiovascular and all-cause mortality. Although this association has been reported for men without prostate cancer, it is still important to keep in mind with regard to men with prostate cancer, because CVD is now the leading cause of noncancer death in men with prostate cancer.[13]

To better inform treatment decisions, particularly for men with advanced disease, more work is needed to

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refine our understanding of the competing risk of CVD mortality in men with prostate cancer. For example, in addition to body composition, cardiorespiratory fitness is an important prognostic measure for all-cause mortality and, within the CVD literature, has been shown to be a stronger risk factor for incident CVD and all-cause mortality than traditional CVD risk factors.[14,15] Emerging data suggest that cardiorespiratory fitness, a physiologic measure that represents the amount of energy used for activity,[16] reflecting a combination of physical activity, genetics, and the overall functional health of various organ systems,[17] is also an important prognostic tool for men with prostate cancer and has previously been demonstrated to be important for men and women with lung and colon cancer.[18]

In this study, weight loss of $< 5\%$ was also associated with an increased risk of death, although as previously noted, because this self-reported weight loss could have been a consequence of illness as opposed to a cause of illness, the authors appropriately caution against causal interpretation. To better understand the associations seen in this study of weight loss $> 5\%$ with increased risk of death, future studies may consider how body mass and weight are captured. As emerging evidence suggests that both fat mass and lean mass are important to health, it is unlikely that BMI alone, which does not distinguish between fat and lean mass, provides a complete picture.[19-21] More work is needed to determine which has more impact on health in men with prostate cancer: the accumulation of fat mass, the loss of lean mass, or a combination. Although this information has been difficult to collect because it required the use of an often cost-prohibitive dual-energy x-ray absorptiometry scan, emerging methods allow for an estimation of body composition from easier-to-collect anthropometrics and routinely collected computed tomography scans.[22,23] Better understanding of the impact of body composition, particularly in the setting of weight change, will inform the types of interventions most beneficial for health.

In conclusion, Troeschel et al[8] highlight the negative impact of obesity and weight gain on outcomes in men with nonmetastatic prostate cancer in their large, prospective cohort study. This study highlights the importance of considering prostate cancer–specific outcomes, as well as CVD outcomes, in men with prostate cancer and highlights areas for future research, including the impact of intentional weight loss and potential roles of fitness and body composition among men with prostate cancer. Furthermore, it emphasizes the increasing need to consider shared risk factors for both cancer and CVD for best management of both diseases.[24]

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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