Obesity and prostate cancer are entities of postmodern medicine. Whereas the modern era ushered in immunizations, aseptic technique, antibiotics and access to clean water, the postmodern era is defined by excess and consumption. Excessive caloric consumption (obesity), excessive antibiotic use and perhaps even excessive screening practices (prostate cancer) are a major part of the landscape of contemporary medicine. The prevalence of obesity has certainly increased substantially in the Western world and is nothing short of an epidemic. With the advent of prostate specific antigen (PSA) testing the incidence of prostate cancer in the United States has climbed steadily and it continues to be the second most lethal malignancy in men. A man in the United States has a 1 in 8 chance of prostate cancer developing and a greater than 70% likelihood of being considered overweight or obese (based on body mass index [BMI]). Because of the tremendous prevalence of both disease entities there has been a growing body of literature on their relationship, and a PubMed® search of both key words will now display 458 articles. In attempting to define the relationship between prostate cancer and obesity several seminal questions must be addressed.

Is Obesity Associated With Prostate Cancer Incidence?
Numerous epidemiological studies have examined the relationship between BMI and prostate cancer risk, and the results have been mixed. Perhaps more convincing is the association of obesity with advanced prostate cancer. The updated Cancer Prevention Study 1 and a subset analysis from the Prostate Cancer Prevention Trial 2 suggest that obesity is positively associated with high risk prostate cancer and negatively associated with low risk disease, which is also consistent with multiple radical prostatectomy series. In other words if you are obese, your risk of prostate cancer may be the same as that of everyone else but you are more likely to have aggressive disease.

Is Obesity Associated With Prostate Cancer Mortality?
Unlike prostate cancer incidence, epidemiological data have consistently shown a positive association between mortality and obesity. The results of the Cancer Prevention Study II indicated that obese men had a 21% increased risk of death from cancer. 3 An 18-year prospective study of 135,006 Swedish construction workers showed a 40% increased risk of death from prostate cancer compared to that of normal weight men. 4 However, these studies did not assess what is arguably the most important confounder affecting prostate cancer mortality: treatment status. In this issue of The Journal Davies et al (page 112) suggest that in surgically treated prostate cancer obesity may not be linked to mortality.

Does Obesity Influence Survival in Surgically Treated Prostate Cancer?
The answer to this question depends on the definition of survival. Most but not all studies in the United States have demonstrated worse biochemical recurrence rates in obese patients as well as worse clinical and pathological features. Davies et al present data from CaPSURE™ involving a community based cohort of more than 7,000 men. They found no relationship between BMI and cancer specific and overall survival, and their findings are similar to those of another study assessing the effect of BMI on extended survival parameters. 5 Obesity appears to be linked to worse clinical and pathological variables but does not appear to impact cancer specific mortality in a surgically treated cohort.

Does Obesity Influence Survival in Metastatic Prostate Cancer?
It depends. In patients with androgen dependant prostate cancer obesity appears to improve overall survival. 6 In cases of androgen independent prostate cancer the data are conflicting. 7,8 Obese patients appear to have lower PSA and alkaline phosphatase levels but whether these are surrogates for survival or simply a result of hemodilution is unknown.

What is the Relationship Between Serum PSA and Obesity?
Also in this issue of The Journal Park et al (page 106) report the results of a large population based study examining the relationship of obesity, PSA
and prostate volume. In using waist circumference as a measurement of total body fat they chose a better surrogate for obesity related metabolic disease and mortality. As in multiple previous series they found a consistent negative association between PSA and obesity (waist circumference and BMI). Obesity was also associated with greater prostate volume. More importantly they demonstrated age adjusted decreases in PSA with obesity even after accounting for prostate volume. The bottom line is that obese men tend to have a larger prostate and lower mean serum PSA, and PSA appears to be low even after adjusting for prostate volume.

This study indirectly raises the thorny issue of PSA screening in obese men. Given that obese men have a lower PSA as well as more aggressive clinical and pathological features, should PSA screening be adjusted based on BMI? Perhaps, but until a study shows worse cancer specific mortality in a screened and treated cohort this change in practice may not be justified. Clearly there is still much to be learned. The most challenging aspect of establishing the interplay between 2 genetically and environmentally complex entities is that we are dealing with 2 moving targets. The epidemiology of obesity and prostate cancer is not the least bit static. Thus, the drive to establish a clear cause and effect relationship may remain elusive.

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REFERENCES


