Obesity is a complex, chronic disease that has reached epidemic proportions in the United States. Obesity is now linked with numerous health conditions, including many oncologic diagnoses. Its association with prostate cancer, the most prevalent cancer in men, has also been investigated, with studies suggesting a direct relationship between increasing obesity and prostate cancer mortality. Outcomes data for specific interventions in obese patients with prostate cancer have only recently begun to emerge. Surgery, while feasible even in the very obese, may result in less than optimal cancer control rates. Brachytherapy data are emerging, and are promising. No outcomes data are available for the use of external-beam radiation in obese patients. Long-term data for external-beam radiation, as well as for surgery and brachytherapy, are required to determine the most appropriate treatment for obese patients with prostate cancer. These data, coupled with a more thorough understanding of the biochemical relationship between obesity and prostate cancer, will be necessary to make optimal management decisions for obese patients with prostate cancer in the future.

In the article entitled "Treatment of Prostate Cancer in Obese Patients," the authors propose that prostate cancer occurring in obese men should be treated differently than that occurring in nonobese men. This proposal is based upon the observation that treatment outcomes in very obese men, to date, are worse than those in men of lesser body mass index (BMI). This may be, in part, due to the technical difficulties encountered in treatment, but is more likely due to a more aggressive disease biology.

Impact of Obesity on Prostate Cancer
The effects of obesity on both prostate carcinogenesis and prostate cancer progression have been the focus of many studies in recent years. Several studies have suggested that very obese men (generally defined as BMI > 35 kg/m²) are more likely to develop prostate cancer,[1,2] but an equal number of studies have suggested the reverse (references 7 and 8 in the article by Mitsuyama et al). In fact, the timing of obesity (and secondary hypogonadism) in a man's life may make a big difference in the effects of obesity on carcinogenesis. Early in life, obesity may be protective, whereas later in life, it may promote a higher risk of prostate cancer (reference 7 in the article). While the effects of obesity on prostate carcinogenesis remain to be fully understood, it is generally agreed by most investigators that prostate cancer occurring in obese men has a more aggressive natural history. Surgical series have demonstrated higher grade, more advanced local stage, and higher likelihood of metastasis among obese men, even when correcting for pretreatment clinical parameters (reference 35 in the article). Cancer-specific mortality rates are higher among obese men developing prostate cancer as well.[3]

As the authors have pointed out, the potential mechanisms underlying the effect of obesity on prostate cancer are multiple. At the core of the potential mechanistic avenues is a significant hormonal dysregulation including decreased testosterone, increased estrogen, and altered fat metabolism. As such, to simply imply that surgery fails in obese men because it is technically more difficult is an oversimplification of a complex biologic process, and it demonstrates a relative naivete regarding prostate cancer therapy.

Diagnosis in Obese Men
The authors suggest technical difficulties of prostate cancer diagnosis in men with obesity. In general, transrectal imaging and needle placement are not greatly affected by obesity. The article by Presti et al referenced by the authors (their reference 27) demonstrated a reduction in cancer detection among obese men with elevated prostate-specific antigen (PSA). Later, however, a reevaluation of the same dataset by Freedland et al demonstrated that when correcting for prostate volume, cancer detection rates were actually higher among obese men.[4]

Obese (and hypogonadal) men with elevated PSA either have a very large prostate or prostate cancer underlying their PSA elevation.[4] They may, in fact, need to be biopsied at lower PSA values in order to overcome the effects of lower testosterone on serum PSA. This illustrates that the
outcomes of the Presti study are more likely affected by the biology of obesity than by the technical difficulties of biopsy in the obese.

**Prostatectomy**
Observations regarding perineal prostatectomy are probably of historical significance only, given the infrequency with which this procedure is performed in contemporary practice. Observations regarding length of operation and blood loss do not translate to clinically significant parameters in measuring morbidity or, more importantly, cancer outcome. Finally, functional outcomes such as continence and potency are highly operator-dependent.

Of more relevance, the authors point out that obese men undergoing radical retropubic prostatectomy are more likely to experience capsular incision, positive margin, and/or biochemical relapse. This appears to be true, even in experienced surgical hands, although operator experience clearly influences this outcome. Nonetheless, the fact that positive margin status and biochemical relapse have never been shown to influence prostate cancer survival make it hard to argue that these factors explain the increased prostate cancer mortality observed in obese men. In fact, the randomized data supporting the use of adjuvant radiation in men with adverse surgical pathology, referenced by the authors, demonstrates no improvement in survival. If it were margin status that predicted survival, this should not be the case. Once again, the biology of obesity (and the aggressive nature of prostate cancer in the obese) appears to affect prostate cancer outcome more than the technical aspects of the treatment.

**Seed Implantation**
The authors appear to suggest that because of the technical difficulties encountered with surgery, seed implantation may provide a better likelihood of disease control in obese men. In this case, they seem to suggest that the relative paucity of data regarding seed outcomes in the obese illustrates treatment superiority. Several points should be made: (1) placement of transperineal needles in obese men is likely more technically difficult than transrectal biopsy; (2) obese men with elevated PSA typically have larger prostates, making seed implantation technically difficult[4]; (3) the single series referenced by the authors has short follow-up, very few obese men, and remains to be validated by others.

Interestingly, in the latter study, the small subset of very obese men did not have higher grade or larger glands—contrary to most reports to date. It is unclear if this cohort is truly representative. More importantly, intuitively, it makes no sense that one focal single-modality therapy would be more efficacious than another for a disease with more likelihood of extraprostatic extension and high grade.

**Conclusions**
Ultimately, it appears clear that single-modality therapy is not doing a good job for obese men with prostate cancer. These men are more likely to have aggressive, extraprostatic disease, and more likely to die of prostate cancer. It is imperative that when redefining treatment paradigms for such men, the oncology community takes into account the disease biology rather than attempting to shift care from one subspecialty to another. Successful treatment approaches for high-risk prostate cancer will require multimodal applications and novel therapies focused on biologic mechanisms of growth control.

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**References:**


