Obesity and Prostate Cancer: Epidemiology and Clinical Implications

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Abstract

Objectives: Both obesity and prostate cancer (PCa) are epidemic in Western society. Although initial epidemiological data appeared conflicting, recent studies have clarified the association between obesity and PCa. Therefore, we sought to review the epidemiological data linking obesity and PCa with an emphasis on the clinical implications and how to improve outcomes among obese men.

Methods: A PubMed search using the keywords “prostate cancer” and “obesity” was performed. Relevant articles and references were reviewed for data on the association between obesity and PCa.

Results: Recent data suggest obesity is associated with reduced risk of nonaggressive disease but increased risk of aggressive disease. This observation may be explained in part by an inherent bias in our ability to detect PCa in obese men (lower PSA values and larger sized prostates, making biopsy less accurate for finding an existent cancer), which ultimately leads to increased risk of cancer recurrence after primary therapy and increased PCa mortality. Despite this detection bias potentially contributing to more aggressive cancers, multiple biological links also exist between obesity and PCa including higher estradiol, insulin, free IGF-1, and leptin levels, and lower free testosterone and adiponectin levels, all of which may promote more aggressive cancers.

Conclusions: The association between obesity and PCa is complex. Emerging data suggest obesity increases the risk of aggressive cancer, while simultaneously decreasing the risk of more indolent disease. This is likely driven by both “biological” and “nonbiological” causes. Simple changes in clinical practice patterns can reduce the impact of nonbiological causes and may help improve PCa outcomes among obese men.

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1. Introduction

Obesity, a rapidly growing worldwide epidemic, is linked to development of numerous types of cancer [1]. In the United States over the last 20 yr, the prevalence of obesity among adults has doubled to 30% (Fig. 1) [2]. Although obesity is less common in Europe, the trend is progressing rapidly, especially in urban areas (Fig. 2) [3].

The reported incidence of prostate cancer (PCa) is highly variable throughout the world owing to multiple factors including PCa screening and access to health care. In the United States, PCa is the most common cancer and the second leading cause of cancer death among men [4]. Globally, PCa is the third most common cancer in men. In industrialized nations, PCa incidence is rising, while mortality is decreasing [5,6]. Decreased PCa mortality also holds true for the European community, with significant reductions in Germany, France, Spain, Italy, and the United Kingdom [6]. Despite the high prevalence of both PCa and obesity, only recently have researchers studied the association between the two in earnest. A PubMed search for “obesity” and “prostate cancer” in March 2007 demonstrated 237 English language papers, of which 177 (75%) were published since January 1, 2001. Thus, three quarters of the world’s literature on this topic was written in the last 6 yr.

Examination of the literature shows that multiple articles suggest obesity promotes, protects, or has no effect on PCa. Therefore, it is tempting to conclude no association exists. However, through separate examination of incidence, progression, and mortality, a clearer picture emerges. Recent data suggest obesity influences all three. Particularly concerning for the clinician is that obesity, as discussed below, is associated with poorer post-treatment outcomes and increased risk of PCa death. Both “biological” and “nonbiological” etiologies are likely involved (Fig. 3). Understanding how obesity influences PCa leads to practical recommendations to improve outcomes among obese men.

Finally, obesity is associated with altered levels of numerous hormones including testosterone, estrogen, insulin, insulin-like growth factor-1 (IGF-1), and leptin, all of which have been linked to PCa (see

Fig. 1 – Prevalence of obesity in adults in the United States. Obesity is represented by the percentage of obese individuals in the population per state. (A) Prevalence of obesity in adults in the United States in 1991. (B) Prevalence of obesity in adults in the United States in 2005.

Fig. 2 – Prevalence of obesity in adults in Europe. Obesity is represented by the percentage of obese individuals in the population of individual countries in 2003.
below). Moreover, obesity is correlated with dietary intake. Obese men have a positive energy balance, and consume greater amounts of dietary fat and simple carbohydrates, all of which are linked with cancer [7]. Obesity is also associated with greater production of inflammatory mediators, and inflammation may be involved in PCA development [8]. A comprehensive review of all of obesity’s sequelae and their relationships to PCA is beyond the scope of this review (Fig. 4). Consequently, we focused on recent studies examining the association between obesity and risk of development, progression following therapy, and death from PCa. Finally, we conclude with clinical advice on how to improve outcomes among obese patients.

2. Methods

An English language literature search using Medline (US National Library of Medicine) and the key words “prostate cancer” and “obesity” identified 237 articles. Of these, 107 were review articles, discussion papers, or letters to the editor. The authors reviewed the final 130 for relevancy; the most recent, pertinent scientific articles were included in the review.

3. Body mass index as surrogate of obesity

Webster’s defines obesity as “a condition characterized by the excessive accumulation and storage of fat in the body” [9]. Both the World Health Organization and the National Institutes of Health define overweight as a body mass index (BMI) $\geq 25$ kg/m$^2$ and obesity as BMI $\geq 30$ kg/m$^2$. BMI (weight in kilograms divided by height in meters squared), while easy to use because only height and weight are needed, has limitations. For example, body composition, such as whether someone has a high lean body mass or is simply large framed is not factored into BMI calculations. Therefore, alterna-
tive measures of obesity including waist-to-hip ratio (WHR), percent body fat, skinfold thickness, crude weight, and lean body mass have been used in various studies.

Importantly, prior studies using BMI and more “precise” measurements of adiposity (ie, WHR) found nearly identical associations for both measurements and often reported only BMI results [10]. The inaccuracy described above is most commonly encountered in large, very muscular individuals with little body fat. These individuals often have an elevated BMI, which could falsely be interpreted as overweight. However, these types of individuals constitute a small part of most populations. Therefore, although BMI is occasionally falsely elevated in some individuals, it remains a reasonably accurate measure of obesity in populations. Although BMI is imprecise, it is the most commonly cited measurement in the literature and therefore the one we primarily refer to in this review.

4. Obesity and risk of PCa diagnosis

Studies examining the relationship between adult BMI and risk of developing PCa have yielded mixed results. Several large cohort studies found increased BMI was associated with an increased risk of PCa [11–14], although some associations were weak. However, other prospective cohort studies found no association between BMI and PCa risk [15,16]. More recently, a prospective cohort study from the United States found an inverse association between obesity and PCa diagnosis, but only among men aged <60 yr or those with a family history [10]. Given these conflicting results, a recent meta-analysis of prospective cohort studies examined this issue and concluded obesity was associated with a significant, but weak, increased PCa risk [17].

Most prior studies examined all PCa cases (ie, not separated by stage or grade). When examined separately by stage and grade, a clearer pattern emerges. Specifically, three recent large prospective studies all reported very similar results. The first two, which collectively followed nearly 400,000 men prospectively, found men with a higher BMI were less likely to be diagnosed with localized disease, but were more likely to be diagnosed with localized high-grade disease [18] or metastatic/fatal disease [18,19]. Moreover, results from the Prostate Cancer Prevention Trial [20] also found that among 10,258 men undergoing biopsy, those with the highest BMI were less likely to have low-grade cancer, but more likely to have high-grade disease.

In light of the protracted course of PCa, perhaps events occurring earlier in life may predispose to PCa later in life. Therefore, examining adult BMI may have missed the window when excess BMI and its sequelae affected PCa risk. The studies examining the relationship between PCa risk and obesity earlier in life have been mixed, with some finding a direct relationship between early life BMI (ages 10–30 yr) and PCa risk [15,21], whereas others found obesity at age 5 yr [22] and 20 yr [23] were protective for PCa. In light of the limited and conflicting data, further research is needed to better assess the association between early life BMI and PCa risk.

In summary, all of the recent large studies suggest adult obesity is associated with decreased risk of low-grade disease, but increased risk of high-grade, advanced disease. The ultimate explanation for this apparent paradox is likely multifactorial. One potential reason, discussed in detail below, is that it may be more difficult to detect PCa in obese men, a phenomenon known as “detection bias.” This detection bias could lead to delayed diagnosis and more advanced stage disease at diagnosis. Importantly, however, the Prostate Cancer Prevention Trial [24] showed similar results in a cohort in which all men underwent biopsy. Thus, as discussed below, although detection bias is a very real possibility, it is unlikely to completely explain the epidemiological association between obesity and PCa risk. Therefore, after we have a thorough understanding of detection bias and its implications, we will discuss the possibility that obesity actually biologically “prevents” low-grade cancer while simultaneously promoting high-grade cancer.

5. Obesity and difficulties in PCa detection

There are several reasons why obesity may make PCa detection more difficult. First, obese men may be less likely to undergo prostate-specific antigen (PSA) testing. However, recent data suggest that, in fact, obese men may actually be more likely to undergo PCa screening [25]. Second, at the time of screening and from our own anecdotal experience, digital rectal examination (DRE) is more difficult in obese men, which could directly result in missing PCa in some obese men that otherwise may have been detected in nonobese men. Therefore, although it is essential to perform thorough examinations in all men, it is particularly relevant in obese men. Third, several reports found obese men have lower PSA values [26–31]. Although one recent report found no association between BMI and PSA in men undergoing screening in Canada [32], this study was small, with a
limited number of obese men. In addition, one study found no association between PSA and BMI among men undergoing radical prostatectomy (RP) [33]; however, with a larger sample size and after controlling for larger prostate size among obese men, the authors did find an association between obesity and lower PSA values [34]. Therefore, the preponderance of the literature to date very strongly suggests obese men have lower PSA values.

With lower PSA values, a bias exists against obese men screened by PSA. However, this bias is relevant in only populations where PSA screening is commonplace (ie, the United States). As other countries adopt PSA screening, obese men in these populations are likely to experience the same screening bias. Furthermore, in present day European countries, the association between obesity and poor outcome may not be as apparent because of both the lower use of PSA screening and the lower overall prevalence of obesity. However, if the trends in obesity continue, we anticipate more disparity in outcomes between obese and nonobese men in these populations in the future.

The reason obese men have lower PSA is currently unknown. One possibility is that obese men have lower testosterone, leading to less PSA production, because PSA production is under androgen control. Alternatively, obese men have greater plasma volume. PSA is normally released in seminal fluid and leaks at low levels into the serum; therefore, greater plasma volume could result in hemodilution, lowering the serum PSA concentration [34]. Regardless of the reason, lower PSA concentrations mean obese men are less likely to have an elevated PSA and subsequently less likely to undergo biopsy, resulting in fewer cancers detected. To overcome this, we correct the PSA value for the degree of obesity. For overweight men (BMI: 25.0–29.9), we multiply PSA by a factor of 1.05, obese Class I (BMI: 30.0–34.9) a factor of 1.1, obese Class II (BMI: 35.0–39.9) a factor of 1.25, and obese Class III (BMI ≥ 40.0) a factor of 1.5 [26].

Several studies also suggested that obese men have larger prostates [35,36]. Most PCas detected by PSA screening are so small they cannot be visualized with conventional imaging. Therefore, prostate biopsy is analogous to looking for a needle in a haystack. Thus, prostatic enlargement (larger haystack) would make detection of an existent cancer (needle) less likely, given an equal sized tumor and an equal number of biopsy cores [37]. To counteract this, we now obtain more cores in obese men. Given that the difference in prostate size in individual patients is often only a few grams, two extra cores will usually suffice. However, a few grams difference across an entire population could lead to as many as 20–25% fewer cancers detected [36].

To illustrate this potential detection bias, we highlight the results from two studies examining the same cohort of 787 men undergoing prostate biopsy to rule out PCa. In the first study [38], the authors found obese men were less likely to be diagnosed with PCa. However, a more thorough review of the patients’ characteristics found obese men were less likely to have abnormal rectal examinations, and had lower PSA values and larger prostates [39]. When these factors were accounted for, obese men were actually more likely to have PCa, and among those with cancer, obese men had higher grade tumors [39].

Importantly, this inherent bias against detecting cancers in obese men is a new hypothesis, although increasing data suggest that we may be missing cancers in obese men. To what degree this hypothesis explains the epidemiological literature is unknown. However, it is our very strong opinion that this detection bias is real and likely has a major influence on the interpretation of the literature regarding obesity and PCa (Fig. 3). Moreover, and most importantly, there are simple steps clinicians can take to overcome this bias. However, the fact that, even when all men are biopsied, obesity is associated with decreased risk of low-grade and increased risk of high-grade cancer strongly supports the fact that biological factors are needed to completely understand the obesity-PCa link [20].

6. Obesity and oncological outcomes after treatment

Several studies found that, among men undergoing primary RP, those with increased BMI had higher-grade disease [40,41]. Although some studies found no link between BMI and oncological outcomes [42,43], most studies [40,41,44–46] did find higher recurrence rates among obese men, including all three studies involving multicenter data [40,41,44]. Moreover, although adding BMI to prognostic models may not markedly improve overall model performance [46,47], it does put the individual obese man at increased risk.

With regard to radiation, whereas one study [48] found no association between BMI and cancer recurrence among men undergoing brachytherapy, another study [49] found that obese men treated with external beam radiation were at increased risk for recurrence and development of metastasis. In light of the limited data, it is unclear whether differences between these studies represent differ-
ences in patient selection, the differential impact of brachytherapy and radiation therapy on obesity-related tumor biology, or alternative explanation(s).

There are several possible reasons, aside from more aggressive tumor biology, that could explain the higher recurrence rates among obese men. One possibility is that, for surgery, obesity may represent a technical challenge such that surgeons are less likely to excise the entire cancer. Indeed, one study found even very experienced surgeons were more likely to have capsular incision when operating on obese men (ie, a technically inferior operation) [50]. Notably, most surgical series found that obese men had an increased risk of positive surgical margins, which likely reflects technical difficulties [40–42]. This increased positive margin risk has been noted in radical retropubic and radical perineal prostatectomy series, and thus appears independent of open surgical approach [51], although this risk has not been well studied in laparoscopic prostatectomy. Technical challenges can also plague radiation. Classically, radiation fields were designed on the basis of a single computed tomography (CT) scan performed prior to starting a 4- to 8-wk radiation course. However, the day-to-day variation in prostate location can result in lower delivered radiation doses, a condition referred to as “setup” error. This daily variance is greater in obese men [52], contributing to a greater setup error, resulting in decreased radiation doses to the prostate and increased complications.

While technical challenges do exist and likely contribute to poorer outcomes, they cannot completely explain the worse outcomes among obese men. For example, prior studies adjusting for increased margin status still found increased recurrence risk after RP [40]. Moreover, even among men with organ-confined disease and negative surgical margins, obesity was linked with recurrence [53]. Ultimately, whether attributable to technical issues, delayed diagnosis resulting in worse disease at presentation, truly inherent biological differences, or a combination of all three, obese men are at increased recurrence risk. This risk should be clearly explained to obese men within the context of its significance on overall mortality risk (see below) and how increased recurrence risk can negatively impact health-related quality of life (HRQOL) (see below).

7. **Obesity and post-RP HRQOL**

In light of the protracted natural history of PCa and the unclear benefit of one treatment over another, it is becoming increasingly clear that other measures such as HRQOL are important end points. Only three studies to date examined obesity and prospectively measured HRQOL in men undergoing RP [54–56]. Two studies found little difference in postoperative HRQOL between obese and normal weight men [54,55]. Specifically, these studies found, by and large, no significant differences in post-RP urinary or sexual function between obese and nonobese men. However, the third study did find that obese men had slower bowel function recovery and increased bother score, although these effects were likely attributable to the greater recurrence risk noted in the study leading to an increased use of secondary treatments, which impact HRQOL [56]. Thus, although only limited data exist, it appears that obesity may not directly negatively affect post-RP HRQOL.

8. **Obesity and risk of PCa death**

Cohort studies prospectively following more than one million cancer-free men consistently found significant associations between increased BMI and risk of PCa death [1,13,57,58]. Additionally, increased BMI has been linked with increased PCa death among men with newly diagnosed PCa [24]. Several large prospective cohort studies deserve particular mention. In 1959 and again in 1982, the American Cancer Society enrolled participants for longitudinal studies on cancer, known as the Cancer Prevention Study (CPS) I and II, respectively. Men were followed for 13 yr in CPS-I and 14 yr in CPS-II. Together, these studies followed 816,268 men, during which time 5212 PCa deaths occurred. Both CPS-I and CPS-II reported obese men (BMI ≥ 30 kg/m²) were 27% and 21% more likely to die from PCa relative to normal weight men, respectively [57]. More details regarding the CPS-II cohort were published, which showed severely obese men were at 34% greater risk of PCa death relative to normal weight men [1]. A prospective study of 135,000 construction workers in Sweden found similar results. Men in the highest BMI category were 40% more likely to die from PCa than men in the lowest BMI category [13]. Finally, a study from Scotland found increased BMI among college students was associated with a 49% increased risk of PCa death, suggesting events involved in prostate carcinogenesis and progression may occur years before actual tumor development [59]. Therefore, there appears to be near uniform consensus among multiple studies involving more than one million men followed prospectively that obesity is associated with increased risk for PCa death.
Of note, the association between obesity and PCa death in the earlier American Cancer Society study was observed in men from the 1950s and 1960s, long before PSA screening [57]. Therefore, the detection bias hypothesis cannot explain the historical association between obesity and PCa mortality. Similarly, neither radiation nor RP were widely used in the 1950s and 1960s because of commonly advanced disease at presentation and excess morbidity. Thus, detection bias issues related to PSA or technical imprecision cannot completely explain the association between obesity and PCa death. Instead, truly biological explanations are needed to completely understand the obesity-aggressive PCa link. Various biological explanations include alterations in serum hormone concentrations, diet, and lack of physical activity (Fig. 4). Almost assuredly, all of these factors play a role, to some degree. Importantly, effects of diet, obesity, and hormonal alterations are all highly interrelated, and a discussion of any one in isolation would be impossible and unrealistic. Therefore, below we give a general overview of each with references provided for more detailed reading.

9. **Hormones, obesity, and PCa**

Adipose tissue not only stores energy, but also functions as an endocrine organ [60]. Adipocytes directly secrete multiple hormones, exerting their signaling effects via endocrine and paracrine pathways (reviewed in [61]). Obesity is also associated with increased serum estradiol levels owing to peripheral conversion of testosterone to estradiol in adipocytes [62]. In turn, estradiol results in feedback inhibition of the pituitary-hypothalamic axis resulting in decreased free testosterone levels [62]. These sex steroid alterations may have profound consequences for PCa development and progression.

Early-stage PCa is exquisitely sensitive to testosterone. However, the exact role of androgens in PCa development remains unclear. Nearly all prospective cohort studies found no significant association between prediagnostic serum testosterone levels and PCa risk [63]. However the optimal time of life to measure serum androgens in evaluating PCa risk is unknown. Most studies have not separately evaluated aggressive and nonaggressive cancers. Testosterone promotes normal prostate epithelium differentiation; therefore, it is possible that lower testosterone activity may also affect tumor differentiation. Indeed, several studies found that, among PCa patients, decreased serum testosterone levels were associated with more advanced and poorly differentiated tumors at presentation [64,65]. Two recent prospective cohort studies concluded that, although no association was observed between androgen levels and total PCa risk, lower prediagnostic serum androgen levels (analogous to obesity) were associated with increased risk for future diagnosis of high-grade PCa [66,67]. It has even been suggested that maintaining normal serum testosterone levels may prevent PCa [68], although this is a very controversial point. Thus, it is possible that lower free testosterone levels in obese men may predispose them to developing more poorly differentiated, advanced PCa, partly explaining higher PCa mortality among obese men. In addition, low testosterone may prevent development of indolent cancers or prevent those that do develop from progressing to the point of clinical detectability, partly explaining the lower risk of localized low-grade disease among obese men.

In addition to alterations in androgens, obesity is associated with increased serum levels of estradiol, insulin, free IGF-1, and leptin, and decreased levels of adiponectin. The relevance of these changes is that all of these steroid and peptide hormones have been linked with PCa [69,70].

Estradiol, when combined with testosterone in animal models, promotes PCa [71–73]. Men in Asia who consume a high soy (phytoestrogen) diet have reduced PCa risks [74]. Finally, a small placebo-controlled, phase 2 clinical trial found that administration of toremifene, which blocks activation of estrogen receptor-α, resulted in a reduced PCa risk [75]. Thus, it is possible that elevated estradiol levels may help contribute to the higher incidence of aggressive PCa in obese men.

Obese men also have elevated insulin levels [62]. Although conflicting data exist [76,77], several studies found that either the metabolic syndrome [78,79], serum insulin [80], fasting glucose levels [81], insulin resistance [82], a high-glycemic index diet [83], or DNA polymorphisms in the insulin gene itself [84] were associated with increased PCa risk. Finally, diabetes is associated with lower serum insulin levels [85]; therefore, the conclusion of a recent meta-analysis [86] that diabetes is inversely associated with PCa risk (relative risk = 0.91, 95% confidence interval, 0.86, 0.96) further supports the link between higher serum insulin and greater PCa risk.

In addition to insulin, some [87,88], but not all studies [89] found that obesity is associated with increased free or bioactive IGF-1. IGF-1 is a potent polypeptide hormone known to stimulate growth of both androgen-sensitive and androgen-independent human PCa cell lines in vitro [90]. Human
studies using prediagnostic serum levels linked elevated IGF-1 with increased PCa risk [91–93]. Moreover, three separate meta-analyses concluded that higher IGF-1 levels were associated with increased PCa risk [94–96]. Thus, elevated IGF-1 levels may represent another biological link between obesity and PCa risk.

Leptin, a hormone produced by adipocytes, is found at higher levels in obese men. In vitro leptin stimulates growth of androgen-independent, but not androgen-sensitive, PCa cell lines [97]. Studies examining associations between leptin levels and PCa risk have been mixed with some finding positive associations [98,99] and others finding no significant association [80,100,101]. Similarly, studies of leptin levels and PCa aggressiveness among PCa patients have been mixed [102–104]. Finally, a recent study found that a particular polymorphism within the leptin gene, associated with increased leptin production and secretion, was associated with increased PCa risk, particularly advanced disease [105]. Although data regarding leptin and PCa are somewhat conflicting, there is a suggestion that leptin may be associated with more advanced, hormone-refractory PCa, possibly explaining another link between obesity and PCa mortality.

Finally, obesity is associated with decreased serum adiponectin, also produced by adipocytes. Although the role of adiponectin in cancer is poorly understood, one study [106] suggested that adiponectin has antiangiogenic properties. Thus, lower antiangiogenic activity among obese men would result in increased angiogenesis and potentially tumor growth. One small nested case-control study [101] found no association between adiponectin levels and PCa risk. However, two studies [107,108] found lower adiponectin levels were associated with more advanced or higher grade PCa, although in one study [107] this association was limited to overweight and obese men. The limited data regarding adiponectin necessitate further study to determine any true biological association between adiponectin and PCa. For more detailed information about specific hormones, obesity, and PCa, we suggest the following reviews: references 63, 69, and 109.

10. **Diet, obesity, and PCa**

A detailed discussion of diet and PCa is beyond the scope of this review; however, we will focus on dietary factors associated with both obesity and PCa, which the clinician should consider.

A drastic change in diet has occurred in many industrialized nations over the last few decades, leading to marked increases in the percentage of overweight and obese individuals. This diet, high in refined carbohydrates, saturated fats (animal meat), and calories, and low in fruits and vegetables is often referred to as a “Western” diet. However, many countries worldwide have begun adopting this dietary trend with subsequent increasing obesity [2,3].

Obesity is the result of multiple factors, most important of which is increased food consumption. Increased total caloric intake has been positively correlated with PCa risk [110]. Furthermore, animal studies have shown that caloric restriction and subsequent weight loss delay PCa growth [111,112]. A prospective cohort study [58] found weight gain was positively associated with fatal or metastatic PCa in certain subsets, whereas another study [18] found that weight loss was associated with decreased PCa risk.

In addition to overall caloric intake, dietary composition also likely plays a role in PCa. Specifically, men in developing countries who adopt a Western diet, which is high in carbohydrates, and saturated and partially hydrogenated fats, and contains fewer protective nutrients such as soy and lycopene, have an increased PCa risk [113]. However, determining which factor(s) within a Western diet contribute to this finding is complex owing to its multifactorial nature. Moreover, the association in humans between PCa and Western diet have been inconsistent, with some showing a positive correlation [113] and others no correlation [114].

Early evidence suggested dietary fat was linked with PCa risk [115] and PCa death [116]. More recently, the specific type of dietary fat has been shown to be important, with saturated fat (ie, animal meat) increasing risk [117–119], whereas polyunsaturated fats may have a protective effect [118]. However, the associations are more complex, in that not only the type of fat but the way food is prepared may influence PCa risk. Specifically, when meat is well cooked (ie, charred), heterocyclic amines (HCA) are created. Animal studies found HCAs increase DNA mutations in prostate tissue [120], leading to PCa development [121]. Furthermore, two human studies [122,123] found consumption of well-cooked meat was associated with higher PCa risk.

Although most studies have examined dietary fat, there is an increased interest in the role of refined carbohydrates. A recent case-control study [118] from Italy found increased PCa risk with higher carbohydrate consumption. It has even been suggested that a low-carbohydrate diet may slow tumor
growth [124], although this is a very controversial matter.

For more detailed information about dietary effects on PCa, we suggest the following reviews: references 125–128.

11. Clinical implications

Several important implications of the above data should be addressed when dealing with the obese patient. First, the fact that obese men have lower PSA levels requires lowering the threshold accordingly for obtaining prostate biopsies (see above). Whether obesity affects PSA velocity, which is increasingly recognized as being important in PCa screening, is unknown. Second, when performing DRE in obese men, special care should be taken to ensure an extensive and complete examination. Finally, because obese men have larger prostates, we advise taking at least two more cores than usual to reduce sampling error. In addition to these PCa-screening issues, obesity can affect outcomes after treatment. Specifically, overweight men should be counseled about the increased recurrence risk after treatment. Recurrences are often treated with salvage therapies that affect HRQOL; therefore, obese men should be counseled regarding the long-term sequelae of these therapies on HRQOL. Finally, obese men are at higher-risk of PCa mortality. These points need to be kept in mind when designing treatment strategies for obese PCa patients. The obese man should be strongly counseled to exercise regularly, eat a balanced diet, and achieve and maintain a healthy weight. This advice is proven to reduce heart disease risk, the overall number one cause of death [4]. Moreover, losing weight has recently been found to reduce the risk of aggressive PCa [18]. Whether weight loss will help improve outcomes among men already diagnosed with PCa is unknown, although this advice is very unlikely to be harmful. Hopefully through a combination of better detection, better treatment, and lifestyle interventions, which actually may help prevent PCa, we can reduce the excess PCa morbidity and mortality among obese men.

Conflicts of interest

Dr Freedland is on the Advisory Board and Speaker’s Bureau for Astra Zeneca and on the Advisory Board for GTX, Inc.

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