The impact of body mass index on prostate cancer

An updated systematic review and meta-analysis

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Abstract

Background: Increasing evidence suggested obesity was associated with the risk of prostate cancer. Also, the association between prostate cancer risk and obesity has received much attention in recent years, but the results are still unclear. Therefore, the current systematic review and meta-analysis aimed to evaluate the impact of body mass index (BMI) on prostate cancer.

Methods: We systematically searched PubMed, Google Scholar, Scopus and Cochrane databases with the appropriate key terms to identify the eligible articles related to the impact of BMI on prostate cancer. The Newcastle-Ottawa checklist was used for the quality assessment of studies, and the meta-analysis was carried out using Review Manager 5.3.

Results: The present review includes 23 studies that fulfilled the criteria for inclusion. In the meta-analysis, a significant difference was observed between the obese and normal weight (P < .001) and 54% of obese has a risk compared to normal weight. Heterogeneity between the fifteen studies was high (I² = 100%). Test for overall effect: Z = 8.77 (P < .001) (odds ratio [OR] = 0.32 confidence interval [CI]: 0.25–0.42). However, there was no significant difference observed between the overweight and normal weight (P = .75). Heterogeneity between the fifteen studies is high (I² = 100%).

Conclusion: Prostate cancer is a common malignancy that poses a threat to the health of men. Obesity is associated with a higher risk of death from prostate cancer based on the findings of the included studies. Furthermore, wherever possible, the impact of weight change on prostate cancer patient mortality should be investigated.

Abbreviations: BMI = body mass index, CI = confidence interval, HR = hazard ratio, OR = odds ratio, PSA = prostate specific antigen.

Keywords: body mass index, obesity, overweight, prostate cancer, risk factor

1. Introduction

In the United States, obesity is a major public health threat, affecting more than 30% of individuals.[1] Obesity rates have more than doubled globally since 1980. Psychological, neuro-endocrine, genetic and environmental factors all have a role in the development of obesity.[2] Obesity is still uncommon in Asian countries such as Japan and Korea, with less than 10% of the population obese, although it has become more common in the recent decade.[2,3] However, recent major investigations have revealed that this link is unclear.[4] Other recognized factors linked to prostate cancer mortality, such as advanced age, a family history of cancer, and ethnicity,[5] are unchangeable. Obesity should be included as a prognosis factor since it is a potentially modifiable factor. Body mass index (BMI) has been associated with many cancers. According to GLOBOCAN 2018, prostate cancer is the third most prevalent cancer in both men and women, as well as the second most common cancer in males worldwide.[6,7] Obesity at a young age delays puberty and may lead to a lower lifetime exposure to insulin-like growth factor 1, which may influence prostate cancer development later in life.[8,9] Elevated lipid levels and lipid signaling, inflammatory responses, insulin resistance, and adipokines have all been proposed as pathways to explain the association between cancer and obesity. However, it remains unclear how the convergence of these pathways drives obesity-linked cancer.[10] Although the advent of prostate specific antigen (PSA) testing has resulted in earlier prostate cancer detection, its significance in lowering prostate cancer-specific mortality is significantly less certain.[11] The impact of potential modifiers of PSA levels, with particular attention focused on obesity, may be represented in the contradictory findings of screening trials. Obese men have...
consistently lower PSA levels in their serum samples than non-obese men.\textsuperscript{12,13}

Obesity may thus have an opposite effect on the incidence of prostate cancer risk in the early stages, depending on the type of prostate cancer. Low testosterone levels in obese individuals could be one of the underlying causes of this inverse relationship between obesity and localized prostate cancer. Due to a reduction in luteinizing hormone pulse amplitude and serum luteinizing hormone levels, obese men have a decreased concentration of free testosterone.\textsuperscript{14} A meta-analysis of 13 studies of advanced prostate cancer and 12 studies of localized prostate cancer found that localized prostate cancer had an inverse linear link with advanced prostate cancer and BMI had a positive linear link with BMI.\textsuperscript{15} Recently, a meta-analysis by Izquierdo et al\textsuperscript{16} reported that obesity was significantly associated with increased specific mortality of prostate cancer. Despite multiple studies suggesting a link between obesity and prostate cancer outcomes, several investigations failed to discover profoundly poor prostate cancer outcomes in a group with a high BMI.\textsuperscript{17,25} Therefore, the current updated systematic review and meta-analysis was performed to identify the impact of BMI on prostate cancer.

2. Methodology

2.1. Study design

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were used for conducting this systematic review and meta-analysis.\textsuperscript{16}

2.2. Search strategy

A literature search was conducted using the relevant keywords and phrases in the following databases: Google Scholar, PubMed, Scopus, and Cochrane. All the published articles up to November 30\textsuperscript{th}, 2021 were included in this review. Different types of keywords were be used for the search strategies such as “body mass index,” “BMI,” “obesity,” “overweight,” “weight,” “adiposity” “weight change” AND “Cancer, prostate,” OR “Prostate cancer,” OR “prostate carcinoma” OR Carcinoma. The bibliographic sources of the selected articles were also screened.

2.3. Inclusion and exclusion criteria

All the published articles were reports with a description of impact of BMI on prostate cancer, measuring BMI at the beginning and then monitoring the incidence of prostate cancer over time, original research articles with all study designs, and articles published in English were included in this review. Studies that evaluated other than prostate cancer, assessing the impact of other comorbidities in breast cancer patients other than BMI; gray literature, including presented abstracts, letters to the editors, commentaries, systematic review or meta-analysis articles and unavailability of the full text of the article were excluded from the review.

2.4. Article screening

Relevant articles were chosen for full-text screening after application of the eligibility criteria. Two authors independently performed the articles screening process and eligibility assessment. In case of some contradictions between the authors, the decision was made by an unbiased third party. The articles were initially screened on the basis of their title, followed by the abstract of the article. In case, the title and abstract of the articles were irrelevant to the present investigation; these were excluded from the secondary screening.

2.5. Data extraction

The followed data were extracted from the selected articles that included: first author, year of publication, country, study design, sample size/gender, age, type of prostate cancer testing, height, weight, BMI, disease stage, confounder adjusted, treatment, follow-up duration, outcome measures and main findings.

2.6. Risk of bias assessment

The study quality was independently assessed by 2 reviewers using the Newcastle-Ottawa checklist. Divergences were solved by a discussion with the third reviewer. The Newcastle-Ottawa checklist was used for the quality assessment of studies. The total score ranged from 0 to 9, while scores less than 3, less than 6 and between 7 and 9 were considered as low, moderate and high-risk studies, respectively.

2.7. Statistical analysis

The meta-analysis was carried out using Review Manager 5.3 (The Cochrane Collaboration, 2014). The total effect size was calculated using a meta-analysis with a 95% confidence interval (CI). Random-effects modeling and generic inverse variance were used to obtain pooled estimates of odds ratio (OR), hazard ratio (HR), and 95% CI, and forest plots were utilized to present the results. Random effects modeling was used because, regardless of the level of statistical heterogeneity. Due to changes in population and treatment, it’s probable that effects differed between trials. The $I^2$ statistic was used to analyze the clinical heterogeneity of included studies using the Cochran Q test. Significant heterogeneity was defined as $I^2$ larger than 50%, and this was discussed accordingly. To identify the source of heterogeneity, sensitivity analysis was performed by assessing the influence of different study features such as sample size, publication year, and menopausal status. Statistical tests were 2-sided, and statistical significance was defined as $P < .05$.

2.8. Ethical considerations

No ethical approval or patient consent was required because all analyses will be based on already published studies. To prevent ethical issues with regards to plagiarism and copyrights, the findings from the selected articles were duly paraphrased along with acknowledging the work of the authors via the addition of references.

3. Results

3.1. Eligible studies

A total of 1226 articles were found in searched databases, including Cochrane, Google Scholar, and PubMed, of which 840 articles were initially eliminated due to repetition and irrelevance. After analyzing the titles and abstracts at the first screening level, 312 articles were further removed. For full-text evaluations, a total of 74 potential relevant articles were chosen, of which 51 articles were further excluded as studies that reported other cancers and disease (n = 24), studies that related to other comorbidities (n = 17) and review articles (n = 10). Finally, this review included 23 studies that matched the criteria for systematic review inclusion as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart (Fig. 1).

3.2. Baseline characteristics study

Table 1 shows the baseline characteristics of the studies that were included. Out of 23 included studies, 8 studies were
published in United States of America, 5 studies in Sweden, 3 studies in the United Kingdom, whereas, the remaining studies were published in different countries, including Germany, Korea, Denmark, Italy, Australia, Netherland and Norway. In addition, the majority of included studies were prospective cohort studies (n = 17), cohort studies (n = 4) followed by population-based cohort study (n = 1) and retrospective cohort study (n = 1). A total of 2702,312 patients were included in the study, with sample sizes ranging between 668 and 336,159. All the included patients in this review were male.

3.3. Risk of bias
The Newcastle-Ottawa checklist was used for risk of bias assessment of the included studies. The risk of bias assessment for each study is shown in Table 2. Among the assessed 23 studies, 12 studies have a “moderate risk,” whereas the remaining 11 studies have a “low risk.” No study was considered to have a “high risk” of bias.

3.4. Impact of BMI on prostate cancer
All the included 23 studies were included for meta-analysis to assess the impact of BMI on prostate cancer. Among the selected 23 studies, the BMI data were classified into 3 groups, including Obese (BMI ≥30), overweight (25 < BMI < 30 kg/m²) and normal weight (<25 kg/m²). The effect of BMI on prostate cancer was assessed in selected studies using the OR and HR. The findings of using the random effects approach to analyze studies revealed that they were heterogeneous.

3.4.1. Overweight vs normal weight. Fifteen studies were included for the Meta analysis for prospective cohort study and retrospective cohort for normal, overweight and obesity. The study reported that there was no significant difference between the overweight and normal weight (P = .75). The study reported that overweight was significantly higher compared with the normal weight. Heterogeneity between the fifteen studies was high (I² = 100%). Test for overall effect: Z = 0.31 (P = .75) (OR = 1.08 CI: 0.66–1.79) (Table 3 and Fig. 2).

3.4.2. Sub-group analysis. Twelve studies were outside the funnel, so we removed those studies and by rerunning the analysis, we got 3 studies for the Meta analysis between normal weight and overweight. A significant difference between overweight and normal weight (P < .001) was found in the study (p0.001). The study reported that obese was significantly higher in the overweight than normal weight (P < .001). Heterogeneity between the 3 studies was medium (I² = 59%). Test for overall effect: Z = 3.96 (P < .0001) (OR = 0.75 CI: 0.65–0.87) (Table 4 and Fig. 3).

3.4.3. Obese versus normal weight. Fifteen studies were included for the Meta analysis of prospective cohort study and retrospective cohort for normal, overweight and obesity. The study reported that there was a significant difference between the normal weight and obese (P < .001). The study reported that obese was significantly higher compared with the normal weight. Heterogeneity between the fifteen studies was high (I² = 100%). Test for overall effect: Z = 8.77 (P < .001) (OR = 0.32 CI: 0.25–0.42) (Table 5 and Fig. 4).

3.4.4. Sub-group analysis. Twelve studies lay outside the funnel, so we removed those studies and by rerunning the analysis, we got 3 studies for the Meta analysis of obese and normal weight. The study reported that there was a significant difference between normal weight and obese (P < .001). The study reported that obese was significantly higher in the obese compared to normal weight (P < .001). Heterogeneity between the 3 studies was medium (I² = 51%). Test for overall effect: Z = 14.37 (P < .0001) (OR = 0.28 CI: 0.23–0.33) (Table 6 and Fig. 5).

3.5. Hazard ratio
Sixteen studies were included for the Meta analysis of prospective cohort study and retrospective cohort for normal,
Table 1
Characteristics of included studies.

| S. No | Author & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Treatment | Follow up duration | Outcome of measures | Main findings |
|-------|-------------|---------|--------------|---------------------|--------------------------------|---------------------------------------|--------------------------------------|----------------------------------|----------------------------------|--------------|-----------------|----------------------|------------|-----------------|------------------|-------------|
| 1     | Vidal et al[17] | USA     | Cohort study | N = 5929/ Male | Median = 60 | Prostate cancer specific antigen testing, Normal Weight (<25) = 7.1 (5.0, 11.0) Overweight (25 to <30) = 6.5 (4.8, 9.7) Obese (≥30) = 6.1 (4.8, 9.2) | NR | NR | Low or normal = 1.00 overweight = 1.16 (0.84–1.62) obese = 1.23 (0.87–1.73) | Early | Multivariate analysis | Age, physical activity, ethnicity, risk factors | NR | 7.4 yrs | Weight, BMI, height | Obesity was found to be associated with an increased risk of PCSM |
| 2     | Jochems et al[18] | Sweden  | A prospective cohort study | N = 431902/ Male | Mean = 69.2 (8.4) | Prostate cancer specific antigen testing, <4 = 2429 (9), 4–9.9 = 10 818 (39), 10–49.9 = 9 402 (34), ≥50 = 4 342 (15) | <173 = 1.00173–176 = 1.01 (0.89–1.20) 1.16177–180 = 1.00 (0.86–1.12) 1.6181–183 = 0.96 (0.83–1.12) >184 = 1.00 (0.85–1.18) | NR | NR | <22.5 = 0.93 (0.79–1.16) 22.5–25 = 1.00 (0.86–1.16) 25–27.4 = 1.12 (0.98–1.28) 27.5–29.9 = 0.98 (0.81–1.17) >/30 = 0.87 (0.68–1.11) | Early | Cox regression | Age, height, BMI, smoking status | NR | 28 yrs | Weight, BMI, height, PSA | BMI was positively associated with PCa-specific mortality |
| 3     | Wissing et al[19] | Germany | A prospective cohort study | N = 1971/ Male | Median = 62 | <5.00 ng/mL = 218 (34.4%) 5.00–7.49 ng/mL = 212 (33.5%) ≥7.50 ng/mL = 197 (31.1%) | NR | NR | 18.5–24.9 (normal weight) = 220 (34.8%) 25.0–29.9 (overweight) = 312 (49.3%) 30.0–34.9 (obesity class 1) = 73 (11.5%) ≥35.0 (obesity class 2–3) = 8 (1.3%) | Localized | Multivariate analysis | Age, BMI, ethnicity, physical activity | NR | 69 mo | BMI, height, PSA | Patients with a higher BMI also had a larger prostate at surgery. BMI and physical activity were not associated with positive surgical margins |
| 4     | Dickerman et al[20] | USA     | A prospective cohort study | N = 5158/ Male | Mean = 40–75 | Prostate cancer specific antigen testing, <4, % = 124–10, % = 57–10+, % = 24 | N = 69.9 (2.6) | NR | <25 kg/m² = 1.00 (ref) 25–≤30 kg/m² = 0.89 (0.71, 1.10) >30 kg/m² = 1.15 (0.81, 1.65) | Localized | Multivariate analysis | Age, height, BMI, smoking status | Radical prostatectomy, Radiation therapy, | NR | BMI, height, PSA | Metabolic changes associated with weight gain may promote prostate cancer progression. | (Continued) |
| S. No | Author & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Treatment | Follow up duration | Outcome of measures | Main findings |
|------|-------------|---------|--------------|---------------------|-----------------------------|--------------------------------------|----------------------------------|--------------------------------|--------------------------------|--------------|----------------|----------------------|-----------|-----------------|-------------------|-------------|
| 5    | Perez-Cor-\-nago et al\[21\] | UK | A prospective cohort study | N = 7024/ Male | Mean = 67.8 | Prostate cancer specific antigen testing | 176.2 cm = 7.2174.3 cm = 7.2172.6 cm = 7.6 | 71.3 kg = 7.382.7 kg = 7.7 97.3 kg = 11.4 | Low or normal = 23.0 (1.6) overweight = 27.2 (1.4) obese = 32.6 (2.7) | Advanced Multivariate analysis | Age, smoking status, physical activity | NR | 13.9 yrs | Weight, BMI | BMI was positively associated with prostate cancer death |
| 6    | Choi et al\[22\] | Korea | A population based cohort study | N = 139,519/ Male | Mean = 40- 64 | Prostate cancer specific antigen testing | NR NR | Low or normal = 0.852 (0.734–0.99) overweight = 1.05 (0.985–1.119) obese = 1.133 (1.067–1.204) | NR Multivariate analysis | Age, smoking status, Alcohol consumption, | NR | 10 yrs | BMI | The hazard ratio (HR) for prostate cancer significantly increased as BMI increases. |
| 7    | Cantaruotti et al\[23\] | Sweden | Cohort study | N = 3161/ Male | Mean = 67 | Prostate cancer specific antigen testing | <172 cm = 197 (20.6)172–175 cm = 226 (23.7)176–179 cm = 215 (22.5)180 cm = 316 (33.2) | <22.5 = 66 (6.7)22.5 < 25 = 75 (5.7)22.5 < 25 = 92 (6.1)27.5 < 68 (254.7) | <22.5 = 21 (1.2) Early | Multivariate Age, height, BMI, Surgery and radiation | 11 yrs | BMI, PSA | BMI, overall mortality | High BMI was associated with a statistically significant increased risk of prostate cancer specific mortality |
| 8    | Møller et al\[24\] | Denmark | A prospective cohort study | N = 26,944/ Male | Median = 56 | Prostate cancer specific antigen testing | 141.5–172.4 cm = 1.00 172.5–176.5 cm = 1.23 (1.08–1.40) 176.8–180.8 cm = 1.23 (1.08–1.41) 181.0–206.0 cm = 1.30 (1.14–1.48) | Low or normal = 1.00overweight = 0.94 (0.85–1.04) obese = 0.86 (0.74–0.99) | NR Early | Multivariate Age, risk group (stage, PSA, BMI) | NR | 15.5 yrs | BMI, height | Obese men with prostate cancer had higher prostate cancer specific mortality |
| 9    | De Nunzio et al\[25\] | Italy | A prospective cohort study | N = 668/Male | Median = 68 (62–73) | Non obese = 6.03 (4.69–NR 8.44)Non obese with central adiposity = 6.46 (4.79–9.21) Obese without central adiposity = 7.1 (5.11–9.53)Obese with central adiposity = 6.2 (4.33–8.77) | NR | Non obese = 25.2NR ± 2.38Non obese with central adiposity = 27.3 ± 1.81Obese without central adiposity = 30.9 ± 1.01Obese with central adiposity = 33.1 ± 3.16 | NR | Multivariate Age, risk group, NR analysis | PSA, BMI | NR | BMI, % waist | Obesity defined by BMI and WC seems to be associated with prostate cancer (CaP) and, more specifically, with high-grade disease at the time of biopsy |
| S. No | Author et al | Country | Study design | Sample size/ Gender | Age (yrs) Range/Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage Type of analysis | Confounders adjusted | Treatment | Follow up duration | Outcome of measures | Main findings |
|-------|--------------|---------|--------------|---------------------|-----------------------------|---------------------------------|----------------------------------|--------------------------------|---------------------------------|----------------------|-----------------|-----------|-------------------|------------------|--------------|
| 10    | Bassett et al | Australia | Prospective cohort study | N = 17,045/ Male | Mean = 27–76 | Prostate cancer specific antigen testing | 167.7 cm to <172.6 cm = 0.97 (0.83, 1.13) | 172.6 to <177.6 cm = 1.04 (0.89, 1.21) | 177.6 cm to <180 cm = 1.04 (0.88, 1.23) | Advanced Cox regression | Age, stage, BMI | NR | 15 yrs | Weight, BMI, Weight gain during adult life is associated with increased prostate cancer mortality. |
| 11    | Stocks et al | Sweden | Prospective cohort study | N = 336,159/ Male | Mean = 34.7 | Prostate cancer specific antigen testing | <173 cm = 1.00 | 173–177 cm = 1.06 (1.01–1.12) | 177–180 cm = 1.10 (1.04–1.17) | Advanced Multivariate analysis | Age, height, BMI, blood pressure | NR | 22.2 yrs | Weight, BMI, BMI and Waist circumference (WC) were also associated with high-grade CaP. |
| 12    | Wallström et al | Sweden | Prospective cohort study | N = 10,564/ Male | Mean = 45–73 | Prostate cancer specific antigen testing | <170 cm = 1.00 | 170–174 cm = 1.20 (0.97–1.49) | 174–178 cm = 1.82 (1.11–1.38) | Advanced Multivariate analysis | Age, waist, BMI, diabetes | NR | 11.0 yrs | % fat, BMI Height was positively associated with total and non-aggressive PCa risk where BMI or body fat percentage, and prevalent diabetes were not associated with PCa risk. |
| S. No | Author & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Treatment | Follow up duration | Outcome of measures | Main findings |
|-------|-------------|---------|--------------|---------------------|-------------------------------|----------------------------------------|-------------------------------------|-------------------------------|--------------------------------|--------------|----------------|---------------------|-----------|-------------------|------------------|--------------|
| 13    | Hernandez et al[29] | USA     | A prospective cohort study | N = 83,879/ Male | Mean = 45–75 | Prostate cancer specific antigen testing | <154 = 1.00154–171.9 = 1.00 172–193.9 = 1.09 ≥ 194 = 1.00 | <66 kg = 1.00 66–67.9 kg = 0.99 (0.91–1.08) ≥ 68–69.9 kg = 0.98 (0.89–1.08) ≥ 70 kg = 1.01 | Under weight = 0.87 (0.66–1.17) Normal = 1.00 overweight = 1.04 (0.97–1.11) obese = 0.94 (0.85–1.04) | Early and localized | Cox regression | Age, ethnicity, BMI | NR | 9.6 yrs | BMI, weight | Evidence that adiposity, as well as increases in adiposity between younger and older adulthood, may influence the development of prostate cancer. |
| 14    | Wright et al[30] | USA     | A prospective cohort study | N = 287,760/ Male | Mean = 50–71 | Prostate cancer specific antigen testing | <25 = 1.78 m 25–29.9 = 1.78 m 30–34.9 = 1.78 m 27.5–39.9 = 1.78 m > 40 = 1.77 m | <58.6 kg = 1.0 58.7–64.5 kg = 1.01 (0.93–1.10) ≥ 64.6–69.9 kg = 0.99 (0.91–1.09) ≥ 70–76.7 kg = 0.99 (0.91–1.09) > 76.7 kg = 0.92 (0.84–1.02) | Under weight = 0.95 (0.87–1.04) Normal = 1.00 overweight = 1.01 (0.95–1.09) obese = 0.93 (0.84–1.02) | Advanced Multivariate analysis | Age, physical activity, BMI | NR | 5 yrs | BMI, height, Weight | Higher BMI and adult weight gain increased the risk of dying from prostate cancer. |
| 15    | Rodriguez et al[31] | USA     | A prospective cohort study | N = 69,991/ Male | Mean = 55–75 | Prostate cancer specific antigen testing | <25 = 70 inch 25–27.5 = 70 inch < 27.5 = 70 inch 30.0–35.0 = 70 inch ≥ 35 = 70 inch | NR | Under weight = 1.00 Normal = 1.02 (0.96–1.09) overweight = 0.98 (0.90–1.06) obese = 0.91 (0.75–1.12) | Advanced Multivariate analysis | Age, smoking status, BMI | NR | 2 yrs | BMI, weight | BMI was positively associated with risk of nonmetastatic high-grade prostate cancer. |
| S. No | Author & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Follow up duration | Outcome of measures | Main findings |
|-------|-------------|---------|--------------|--------------------|-----------------------------|----------------------------------|---------------------------------|-----------------------------|-------------------------------|---------------|----------------|--------------------|----------------|----------------|--------------|
| 16    | Kurahashi et al[32] | UK | A prospective cohort study | N = 49 850/ Male | Mean = 40–69 | NR | <159 = 1.0 cm | 160–164 = 0.97–1.76 | cm 164–167 = 0.94–1.80 | cm > 168 = 0.82–1.66 cm | Under weight = 1.00 Normal = 0.77–1.44 overweight = 0.87–1.65 obese = 0.97–1.76 | Advanced Multivariate Age, risk factors, BMI analysis | NR | BMI, height | No evidence that BMI is associated with the risk of prostate cancer |
| 17    | Engeland et al[33] | UK | Cohort study | N = 951 459/ Male | Mean = 44.5 | Prostate cancer specific antigen testing | <160 = 0.64 (0.57–0.73) 160–169 = 0.89 (0.87–0.92) 170–179 = 1.00 180–189 = 1.06 190–196 = 1.11 (0.99–1.24) | Under weight = 0.92 (0.78–1.08) Normal = 1.00 overweight = 1.07 (1.05–1.09) obese = 1.09 (1.04–1.15) | Advanced Cox regression: Age, BMI | NR | 21 yrs | BMI, height | The risk of prostate cancer increased by both BMI and height. |
| 18    | Lee et al[34] | USA | A prospective cohort study | N = 8922/ Male | Mean = 67 | NR | <86.4 | 86.4–91.4 = 1.30 (0.96–1.76) 91.5–96.5 = 1.31 (0.96–1.80) > 96.5 = 1.19 (0.85–1.65) | Under weight = 1.00 Normal = 1.27 (0.94–1.71) overweight = 1.26 (0.92–1.72) obese = 1.02 (0.68–1.53) | Multivariate Age, BMI, weight | NR | BMI, Weight | BMI did not yield any significant association with prostate cancer |
| S. No | Author(s) & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Treatment | Follow up duration | Outcome of measures | Main findings |
|-------|----------------|---------|--------------|---------------------|------------------|--------------------------------|------------------|------------------|------------------|-------------|----------------|------------------|-----------|------------------|------------------|--------------|
| 19    | Schuurman et al[35] | Netherlands | Cohort study | N = 58,279/ Male | Mean = 55-69 NR | <170 = 1.00 170–174 = 0.90 (0.65–1.24) 174–179 = 1.08 (0.79–1.47) 180–184 = 0.98 (0.70–1.37) 185–189 = 0.78 (0.51–1.19) >190 = 0.96 (0.52–1.75) | NR | <69.5 = 1.070.0–75.0 = 0.8 (0.7–1.3) 75.5–80.5 = 1.0 (0.8–1.2) 81.0–87.0 = 1.1 (0.9–1.4) >87.5 = 1.0 (0.8–1.3) | NR | Under weight = 1.00 Normal = 1.20 overweight = 1.35 obese = 0.89 (0.84–1.73) (0.95–1.90) (0.58–1.57) | Advanced Multivariate Age, BMI, analysis | BMI, height | NR | 6.3 yrs | Results do not indicate a strong association between body mass index (BMI) and risk of prostate cancer. |
| 20    | Nilsen and Vatoren[36] | Norway | A prospective cohort study | N = 22,248/ Male | Mean = 75.2 (48-96 years) | <169 = 1.0170–173 = 1.1 (0.9–1.3) 174–176 = 1.2 (0.9–1.5) 177–180 = 1.3 (0.9–1.7) >181 = 1.3 (0.9–1.9) | NR | <23.0 = 1.023.0–24.7 = 0.8 (0.6–1.0) 25.0–26.2 = 1.1 (0.9–1.3) 27.0–28.2 = 0.9 (0.7–1.2) 29.0–30.0 = 1.0 (0.8–1.2) | NR | Advanced Multivariate Age, BMI, analysis | BMI, height | NR | 12 yrs | Results do not indicate a strong association between body mass index (BMI) and risk of prostate cancer. |
| 21    | Giovannucci et al[37] | USA | A prospective cohort study | N = 47,781/ Male | Median = 20-40 | <66 inch = 1.0 66 inch = 1.09 (0.91–1.30) 68 inch = 1.07 (0.91–1.27) 70 inch = 1.08 (0.90–1.30) 72 inch = 0.98 (0.80 –1.19) 73 inch = 1.22 (0.97–1.59) >74 inch = 1.37 (1.10–1.70) | NR | <23.0 = 1.023–24.9 = 1.25 (1.03–1.51) 25–26.9 = 1.05 (0.87–1.28) 28–29.9 = 1.11 (0.90–1.36) >29 = 0.90 (0.71–1.15) | NR | Advanced Multivariate Age, BMI, analysis | BMI, height | Childhood obesity have a strong influence on prostate carcinogenesis. | 2 yrs | BMI, height | Childhood obesity have a strong influence on prostate carcinogenesis. |
| S. No | Author & yr | Country | Study design | Sample size/ Gender | Age (yrs) Range/ Mean/ Median | Type of Prostate cancer testing (ng/mL) | Height [HR: 95% conf. interval] | Weight [HR: 95% conf. interval] | BMI range [HR: 95% conf. interval] | Disease stage | Type of analysis | Confounders adjusted | Follow up duration | Outcome of measures | Main findings |
|-------|-------------|---------|--------------|---------------------|-----------------------------|--------------------------------------|-------------------------------------|---------------------------------|----------------------------------|--------------|----------------|---------------------|-----------------|----------------|----------------|
| 22    | Cerhan et al[38] | USA     | Prospective cohort study | N = 1050/ Male       | Mean = 73.5 (65 - 101) | <173 = 1173–177 = 0.8 (0.4–1.4) | <70.8 = 170.8–180 = 0.6 (0.3–1.2) | >0.80 = 1.1 (0.6–2.0) | <23.6 = 123.6–25.8 = 0.8 (0.4–1.8) | Early | Multivariate Age, smoking status, physical activity | NR | 10 yrs | BMI, height, Greater BMI was independent predictors of prostate cancer |
| 23    | Andersson et al[39] | Sweden  | Retrospective cohort study | N = 135,049/ Male    | Mean = 30 - 60 | <172 = 1.0172–176 = 1.069–75 = 1.05 (0.95–1.16) | <69 = 3 = 1.05 (0.93–1.19) | >0.80 = 1.14 (1.00–1.29) | <22.1 = 1.022.1–24.1 = 1.09 (0.94–1.26) | Early | Multivariate Age, BMI, weight | NR | 20 yrs | BMI, height, The excess risk of death from prostate cancer was statistically significant in all BMI categories |

UK = United Kingdom, USA = United States of America.
overweight and obesity. The study reported that there was significant difference between the normal weight and obese ($P = .009$). Heterogeneity between the fifteen studies was high ($I^2 = 0\%$). Test for overall effect: $Z = 2.59$ ($P = .009$) (HR = 1.03 CI: 1.01–1.05) (Table 7 and Fig. 6).

4. Discussion

Prostate cancer is the second most frequent cancer among men throughout the world.$^{[7]}$ The link between BMI and mortality in prostate cancer patients has been associated with a number of causes. In this review, 23 studies comprising 2702,312 patients were included to explore the relationship between the risk of prostate cancer and BMI. There was no significant difference observed between the normal weight and overweight ($P = .75$) (OR = 1.08 CI: 0.66–1.79) and the heterogeneity between the fifteen studies was high ($I^2 = 100\%$). However, after removing the publication bias in sub-group analysis, there was a significant difference between normal weight and overweight ($P < .001$). High BMI at a young age was negatively associated with overall risk of prostate cancer, according to a prospective analysis of 141,896 males in the European Prospective Investigation into Cancer and Nutrition cohort, as well as fatal and advanced illness,$^{[8]}$ which is similar to the findings of a review. In this review, there is no significant difference observed between the normal weight and obese ($P < .001$) (OR = 0.32 CI: 0.25–0.42) and the heterogeneity between the fifteen studies is high ($I^2 = 100\%$). Similarly, after removing the publication bias in sub-group analysis, there was a significant difference between normal weight and overweight ($P < .001$).
review by Harrison et al.\textsuperscript{19} observed no evidence of an association between BMI and the risk of prostate cancer, which is a contrast to our present findings. However, a meta-analysis by Cao and Ma\textsuperscript{20} detected high heterogeneity among the studies reviewed in the present analysis. The stratified meta-analyses revealed a clear and persistent link between BMI and increased prostate cancer mortality. Similarly, a meta-analysis of 13 advanced prostate cancer studies and 12 prostate cancer studies found that localized prostate cancer had an inverse linear connection with BMI and advanced prostate cancer had a positive linear link with BMI.\textsuperscript{15}

The present review has some limitations. Firstly, we used subgroup analysis to find the major source of heterogeneity after observing it across studies. Secondly, the lack of data of confounding factors in the analysis of data such as cigarette smoking or age. Thirdly, unmeasured variables linked to BMI may have altered the outcomes of individual research, even though many of the studies had adjusted for key risk factors. Despite these limitations, this updated systematic review and meta-analysis provides an evidence-based report on the impact of BMI on prostate cancer demonstrated by pooled effect of different studies using rigorous methodology.
5. Conclusion

In conclusion, according to the findings of the studies examined, a greater BMI is linked to a higher risk of prostate cancer. Future studies will evaluate the influence of BMI on patient mortality in prostate cancer patients should be stratified by cancer type, with well-controlled confounding variables including disease duration, therapy, and lifestyle. Furthermore, wherever possible, the impact of weight change on prostate cancer patient mortality should be investigated.

**Author contributions**

Data curation: Mohamed Chahine.
Methodology: Mohamed Chahine.
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Writing – review & editing: Mary E. Tazanios.
**Table 7**

Forest plot for the association between BMI (obese vs normal weight) and prostate cancer (hazard ratios).

| Study or Subgroup | Cases | Control | Total | O.E. Variance | Weight |
|-------------------|-------|---------|-------|---------------|--------|
| A. England et al. 2003 | 5200 | 39500 | 33300 | 38500 | 103.62 | 4,497.86 | 55.5% |
| Anderson et al. 1997 | 708 | 3073 | 2364 | 3073 | 20.43 | 544.83 | 8.7% |
| Bassett-Jr. et al. 2012 | 140 | 5550 | 15140 | 15550 | 10.46 | 103.91 | 1.3% |
| Cantarutti et al. 2015 | 658 | 2592 | 1934 | 2592 | 7.13 | 490.96 | 6.1% |
| Dickerman et al. 2017 | 371 | 5158 | 4787 | 5159 | 9.25 | 346.11 | 4.3% |
| Giovannucci et al. 1997 | 447 | 4891 | 46412 | 48919 | 1.44 | 120.99 | 1.8% |
| Lee et al. 2001 | 34 | 473 | 439 | 473 | 1.54 | 31.566 | 0.4% |
| Moller et al. 2014 | 290 | 2103 | 1813 | 2103 | 14.89 | 250 | 3.1% |
| Nair, T. et al. 2002 | 91 | 493030 | 49539 | 49330 | 1.2915 | 76.4 | 0.9% |
| Perez-Cornago et al. 2017 | 1384 | 141896 | 140512 | 141896 | 27.45 | 557.66 | 6.9% |
| Rodriguez et al. 2007 | 288 | 69991 | 63184 | 69991 | 10.86 | 58.66 | 0.7% |
| Schouten et al. 2000 | 228 | 2248 | 2190 | 2248 | 4.3886 | 204.95 | 2.5% |
| Stocks et al. 2010 | 2492 | 323559 | 326157 | 323559 | 7.21 | 105.18 | 1.3% |
| Vidal et al. 2020 | 181 | 5929 | 5748 | 5929 | 0.3712 | 39.79 | 0.5% |
| Wahlström et al. 2009 | 281 | 15554 | 9741 | 10564 | 0.264 | 504.6 | 6.2% |
| Wright et al. 2007 | 1448 | 297220 | 277774 | 297220 | 12.26 | 124.51 | 1.9% |

**Figure 6.** Funnel plot of hazard ratio estimates of prostate cancer by obese versus normal weight.

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