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ASSOCIATION OF SMOKING AND PROSTATE CANCER : A 10 YEARS SYSTEMATIC REVIEW

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ABSTRACT

Background: *Prostate cancer (PCa) is the second most commonly diagnosed cancer and the fifth leading cause of cancer death among males, with an estimated 1.4 million new cases and 375 000 deaths worldwide in 2020, accounting for 7.3% and 3.8% of all cancers diagnosed, respectively. Various endogenous and exogenous risk factors for PCa have been discussed for decades. Several factors have been identified to be associated with an increased risk of PCa, for instance, family history, elevated hormone levels, black ethnicity, and high alcohol consumption.*

The aim: *This study aims to show about association of smoking and prostate cancer.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 30 articles, whereas the results of our search on SagePub brought up 55 articles. The results of the search conducted for the last year of 2014 yielded a total 13 articles for PubMed and 23 articles for SagePub. The result from title screening, a total 10 articles for PubMed and 15 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.*

Conclusion: *Regarding smoking, burning tobacco and inhaling the smoke is considered a significant risk factor or direct cause of cancer, tumor lesions, and a well-known chemical carcinogen.*

Keyword: *Prostate cancer, smoking, carcinogen.*

INTRODUCTION

The medical community and the general public generally accept that cigarette smoking is a major determinant of mortality. Perhaps less appreciated, a pooled analysis of nearly one million people found that 17% of this excess mortality was due to causes of death not typically associated with smoking, including prostate cancer. The 2014 Surgeon General's report found current or recent smoking was associated with an increased risk of advanced-stage prostate cancer and death from prostate cancer, although not associated with overall incidence of the disease. Because the specific compounds in cigarettes that most strongly influence prostate cancer outcomes have not been identified, it is not clear the extent to which other tobacco products, some of which are increasing in popularity, also pose risks.[1]

Globally, prostate cancer (PCa) is the second leading cause of cancer and the fifth leading cause of cancer mortality among men worldwide. The burden of PCa is predicted to grow by nearly around 2.3 million incidences and 740000 deaths worldwide by 2040[2]. In the USA, there were an estimated 248530 new cases and 34130 deaths from PCa in the year 2021. The reported incidence of PCa in developing countries is lower than in the developed countries. It is not clear what the reason is; however, it might be due to underreporting from diagnosing centers to the national cancer registry and the geographical variation reflected by ethnic and racial dissimilarity. Worldwide the incidence of PCa has increased remarkably, which might be attributed to the increased screening uptake among men for prostate-specific antigen (PSA) without disease symptoms.[2,3]

Smoking is a well-established risk factor for several cancers, such as lung cancer, head and neck cancer, bladder cancer, and esophageal cancer. However, the data on the association between smoking and PCa incidence are conflicting. In a meta-analysis of 24 prospective cohort studies, M. Huncharek showed that current smokers had no increased risk of incident PCa, but in data stratified by amount smoked, a significant elevated risk was observed, and former smokers had a higher risk of PCa in comparison with never smokers. Another meta-analysis conducted in 2014 revealed an inverse association between current smoking and PCa risk, while in studies completed before the prostate-specific antigen (PSA) screening era, ever smoking was positively associated with PCa. In addition, a recent pooled study of five Swedish cohorts demonstrated that former smokers and current smokers had a lower risk of PCa than never smokers, and smoking intensity was inversely associated with PCa risk, especially in the PSA screening era.[4]

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we compare and contrast association of smoking and prostate cancer. It is possible to accomplish this by researching or investigating association of smoking and prostate cancer. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about association of smoking and prostate cancer. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used " association of smoking and prostate cancer." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("*Impact of smoking*"[MeSH Subheading] OR "*Prostate cancer*"[All Fields] OR "*Mechanism of prostate cancer*" [All Fields]) AND ("*Correlation of smoking and prostate cancer*"[All Fields] OR "* Incident of prostate cancer *"[All Fields))* used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

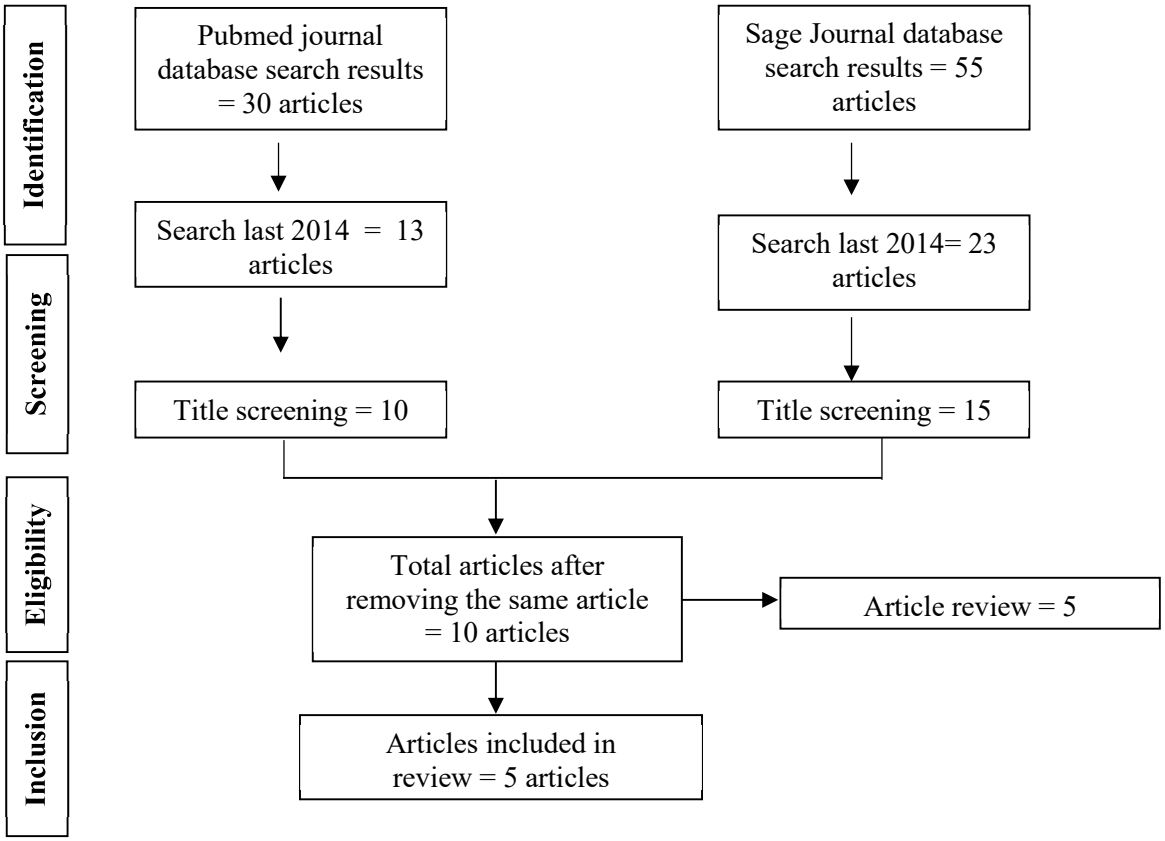

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 30 articles, whereas the results of our search on SagePub brought up 55 articles. The results of the search conducted for the last year of 2014 yielded a total 13 articles for PubMed and 23 articles for SagePub. The result from title screening, a total 10 articles for PubMed and 15 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

Khan, S *et al* (2019)[5] showed A longer smoking duration is significantly associated with an increased risk of biochemical recurrence among ever-smokers with prostate cancer. Increased pack-years of smoking exposure may also be associated with biochemical recurrence. Smoking duration is a modifiable risk factor and could be used to identify the ever-smokers at highest-risk for prostate cancer recurrence.

Mendoza, EJ *et al* (2018)[6] showed that the association between smoking and PC is complex, and could depend on changes in smoking intensity over the life course. The prevalence of smoking pattern B among controls living in Mexico City was 7.4%; assuming that controls represent the general male population, approximately 9% of poorly differentiated PC (Gleason ≥8) could be attributable to life course smoking pattern B. Inconsistencies observed in previous studies could

respond to disregard for PC aggressiveness and limitations of exposure assessment methods. Using smoking patterns throughout life course could help us understand the link between smoking and PC, but further validation of the method is needed, particularly in the context of prospective studies with different smoking prevalence and intensity than ours.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Khan, S *et al*., 2019[5]	USA	Prospective cohort study	1641	In the full cohort, we observed no association between ever-smoking and risk of biochemical recurrence. However, among ever-smokers a smoking duration of ≥ 10 years was significantly associated with biochemical recurrence (Hazard Ratio (HR): 2.32, 95% Confidence Interval (CI): 1.01, 5.33). Our results also suggested that ≥ 10 pack-years of smoking may be associated with an increased risk of biochemical recurrence (HR: 1.75, 95% CI: 0.97, 3.15). No association was observed between packs smoked per day or years since smoking cessation (among former smokers) and risk of biochemical recurrence.
Mendoza, EJ *et al*., 2018[6]	Mexico	A case-control study	402	Two life-course smoking patterns were identified among ever smokers: "pattern A" characterized by males who reported low and constant smoking intensity (87.8%), and "pattern B" (12.2%) males with an initial period of low intensity, followed by an increase during the second period. Compared to never smokers, pattern B was associated with higher poorly differentiated PC, (OR 2.30; 95% CI 1.21–4.38). No association was observed with average smoking index.
Ho, T *et al*., 2014[7]	USA			Of 6,240 men with complete data and ≥1 on-study biopsy, 2,937 (45.8%) never smoked, 929 (14.5%) were current smokers, and 2,554 (39.8%) were former smokers. Among men with negative first on-study biopsies, smokers were 36% less likely to receive a second on-study biopsy ($p<0.001$). At first on-study biopsy, 941 (14.7%) men had cancer. Both current and former smoking were not significantly associated with either total or low-grade prostate cancer (all $p>0.36$). Current (OR=1.44, $p=0.028$) but not former smokers

				(OR=1.21, p=0.12) were at increased risk of high-grade disease. On secondary analysis, there was an interaction between smoking and BMI (p-interaction=0.017): current smokers with BMI ≤25 had increased risk of low- (OR=1.54, p=0.043) and high-grade disease (OR=2.45, p=0.002), with null associations for BMI ≥25.
Moreira, DM *et al*., 2014[8]	USA	Retrospective study	549	A total of 549 men (33%) men were active smokers and 1121 (67%) were nonsmokers at the time of surgery. Current smokers were younger and had a lower body mass index, higher prostate-specific antigen level, and more extracapsular extension and seminal vesicle invasion (all P <.05). A total of 509 patients, 26 patients, 30 patients, 18 patients, and 217 patients, respectively, experienced BCR, metastasis, CRPC, prostate cancer-related death, and any-cause death over a median follow-up of 62 months, 75 months, 61 months, 78 months, and 78 months, respectively. After adjusting for preoperative features, active smoking was found to be associated with an increased risk of BCR (hazards ratio [HR], 1.25; P =.024), metastasis (HR, 2.64; P =.026), CRPC (HR, 2.62; P =.021), and overall mortality (HR, 2.14; P <.001). Similar results were noted after further adjustment for postoperative features, with the exception of BCR (HR, 1.10; P =.335), metastasis (HR, 2.51; P =.044), CRPC (HR, 2.67; P =.015), and death (HR, 2.03; P <.001).
Kao, YH *et al*., 2019[9]	USA	A cross-sectional study	354	This study found that 33.2% (n=111) of prostate cancer survivors had an elevated NLR. Prostate cancer survivors with a high NLR were older (mean 73.5 years old), non-Hispanic white (38.5%), higher income (poverty income ratio >1, 34.7%), and longer years after diagnosis (8.8 years) compared to counterparts with a low NLR. Smoking status did not have a

				significant impact on NLR. The interaction test between race and smoking status was significant (P=0.04). Non-Hispanic black who were current smokers were observed more likely to have high NLR than never smokers [adjusted odds ratio (OR) =3.69, 95% CI: 1.36–9.99]. However, the effect of smoking on NLR was not observed among either non-Hispanic whites or other races.

Ho T *et al* (2014)[7] showed Among men with an elevated PSA and negative pre-study biopsy in REDUCE, in which men were instructed to receive biopsies independent of PSA levels, cigarette smoking was related to poor study biopsy compliance. At first on-study biopsy, smoking was unrelated to overall prostate cancer diagnosis or low grade disease. However, current smoking was associated with increased risk of high grade prostate cancer diagnosis in lean men.

Moreira, DM *et al* (2014)[8] showed Among patients undergoing radical prostatectomy, cigarette smoking was associated with an increased risk of metastasis. In addition, smoking was associated with a higher risk of BCR, CRPC, and overall mortality. If confirmed, these data suggest that smoking is a modifiable risk factor in patients with aggressive prostate cancer.

Kao, YH *et al* (2019)[9] showed non-Hispanic black prostate cancer survivors who currently smoked were more likely to have high NLR levels than never smokers. We recommend that intervention programs that aim to provoke smoking cessation among prostate cancer survivors should primarily focus on non-Hispanic black population. In addition, non-Hispanic black prostate cancer survivors who smoke should be encouraged to stop smoking, as this might benefit prostate cancer management and reduce the risk of cancer progression.

DISCUSSION

Burning tobacco products and its additives produces thousands of chemicals, including more than 70 well-known carcinogens. Tobacco smoking is known as a preventable risk factor for the development and mortality of several genitourinary cancers such as bladder cancer, upper tract urothelial carcinoma, and renal cell carcinoma. In contrast, the effect of tobacco consumption on the incidence of prostate cancer is still a matter of debate. Nevertheless, the association between cigarette smoking and prostate cancer mortality seems to be robust. Two meta-analyses that evaluated the association of smoking with prostate cancer outcomes confirmed a higher risk of death among current smokers than among nonsmokers. These apparently discordant findings could be explained by the presence of higher-grade or higher-stage disease at the time of diagnosis, the adverse effects of tobacco use on oncologic outcomes after primary treatment, or both. Some studies revealed a correlation between smoking status and higher tumor volumes, more expansive high-grade tumor volumes, and extracapsular extension during radical prostatectomy (RP).[10]

The association between smoking tobacco and urologic cancers has been extensively studied. While it is well known that smoking is among the leading predisposing factors for bladder cancer, prostate cancer, renal cancer, and upper tract urothelial cancer (UTUC), the impact of smoking tobacco can be manifold as it may affect several stages in cancer therapy. In addition to tumorigenesis, smoking may also lead to poor surgical outcomes, prolonged recovery periods, increased complication rate, poor response to chemotherapy, and potentially have an impact on recurrence. Studies and publications regarding urologic cancers and smoking have gradually been on the rise over the last fifty years.[11]

Prostate cancer (PCa) is the second most diagnosed cancer in men worldwide. Many potential risk factors for prostate cancer have been studied. Current smoking status has not explicitly been linked with tumorigenesis. The most recent report by the Surgeon General in 2014 concluded that “the evidence is suggestive of no causal relationship between smoking and the risk of incident prostate cancer.” However, while the existence and mechanism of an etiologic link between smoking and prostate cancer is unclear, there have been several proposed mechanisms. The prevalent hypothesis involves the mutation of various cancer progression genes by tobacco-related carcinogens. Other proposals involve inflammatory response, hormone alterations, proliferation of tumor angiogenesis, and immune suppression.[11,12]

As was documented, younger male patients with early-onset PCa have risen over the past 3 decades, and had the highest mortality among all age groups, since they were inclined to have a higher risk or metastatic form. However, our results showed that the proportion of prostate cancer mortality attributable to smoking in patients younger than 55 years remained stable. This may be due to lower smoking prevalence and the shorter duration of exposure to smoking in those age groups. Moreover, our research also indicates a slight increase in the proportion of cancer-specific mortality rates attributable to smoking among older adults older than 75 years. This was probably due to the lag between stopping smoking and

developing prostate cancer. The cohort born between 1955–1965 (aged 35–44 years in 2000) was the first cohort to experience a significant decline in smoking prevalence, from 32.0% in 2000 to 21.1% in 2020, while the cohort born before that time remained almost stable over time.[13,14]

CONCLUSION

Regarding smoking, burning tobacco and inhaling the smoke is considered a significant risk factor or direct cause of cancer, tumor lesions, and a well-known chemical carcinogen. smokers have an increased risk of death from prostate cancer. Important to realize that this lower risk for smokers might be attributed to low prostate cancer screening uptake among smokers, misclassification bias, or selection bias from the included original studies. In summary, our results indicate that the incidence of prostate cancer is lower among smokers. Nevertheless, smokers who develop the disease have a significantly worse prognosis.

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