World Cancer Research Journal WCRJ 2017; 4 (4): e972

THE INCIDENCE, RISK FACTORS, AND KNOWLEDGE ABOUT THE PROSTATE CANCER THROUGH WORLDWIDE AND IRAN

H.R. SADEGHI-GANDOMANI[1,2], M.S. YOUSEFI[3], S. RAHIMI[4], S.M. YOUSEFI[5], A. KARIMI-ROZVEH[6], S. HOSSEINI[7], A.A. MAHABADI[8], H.F. ABARQUI[8], N.N. BORUJENI[1], H. SALEHINIYA[1,9]

[1]Zabol University of Medical Sciences, Zabol, Iran
[2]Trauma Nursing Research Center, School of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran
[3]School of Nursing and Midwifery, Qom University of Medical Sciences, Qom, Iran
[4]Department of Nursing, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
[5]Trauma Nursing Research Center, School of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran
[6]School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran Iran
[7]School of Nursing and Midwifery, Gorgan University of Medical Sciences, Gorgan, Iran
[8]School of Medicine, Kashan University of Medical Sciences, Kashan, Iran
[9]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Abstract – *Objective:* *The aims of this review study were to provide awareness about PCa as well as an updated knowledge about the incidence, risk factors, and knowledge of PCa in Iran and all over the world.*

Materials and Methods: *A rapid literature search strategy was conducted for all English language literature published before March 2017. The search was conducted using the electronic database PubMed, Embase, Scopus and Web of Sciences. The search strategy included the keywords 'prostate cancer', 'epidemiology', 'incidence', 'mortality', 'risk factor', 'survival, 'Iran', and 'worldwide'.*

Results: *Incidence rates are relatively high in certain less developed regions. The lowest incidence rates are observed in Central and Eastern European countries and also in Asian populations. Mortality rates are generally high in predominantly black populations. The main risk factors associated with PCa are as follow: smoking and drinking, low intake of fresh fruit and vegetables, geographical area, family medical history, genetic changes, race/ethnicity, occupation, excessive use of micronutrient, estrogen metabolism, obesity, inflammation of the prostate, vasectomy and sexual activity/sexually transmitted diseases.*

Conclusions: *This study may provide considerable evidence for PCa's major and minor risk factors. This may be helpful in identifying subsets of the population who are more at risk of developing PCa. Effective preventive actions, such as health education, nutritional intervention, and screening programs, are needed especially in high-risk areas of the world.*

KEYWORDS: *Prostate cancer, Incidence, Mortality, Risk factors, Iran, World.*

Corresponding Author: Hamid Salehiniya, MD; e-mail: alesaleh70@yahoo.com

INTRODUCTION

Prostate cancer (PCa) is the second most common cancer and the sixth leading cause of cancer death among men worldwide, with an estimated recorded amount of 1.1 million cases and 307,000 deaths in 2012[1,2], which allocates 15% of all new cases of cancer in men (3). Prostate cancer sufferers are the diagnosed men, (almost 70% of the cases numbered: 759,000) in more developed regions[1]. Approximately, 42% of PCa cases occur in men over the ages of 50 years old and the majority of them are often seen after 60 years old[4]. Few studies have been implemented about the epidemiology of PCa in Iran[4,5], although it is the second most common cancer in men and the sixth most common cancer in Iran[6]. Therefore, PCa has become an important public health concern as a chronic disease[3].

Epidemiologic studies have shown that there are geographical and racial distribution differences about PCa; it happens more often in Western countries than Asian ones, such as Iran[7-9]. The considerable geographical variation demonstrated that different causal factors are influencing the increasing of PCa rate. Therefore, this study aimed at investigating the incidence, risk factors and the knowledge about PCa in Iran and worldwide.

METHODS

A rapid literature search strategy was conducted for all English language literature published before March 2017. The search was conducted using the electronic databases PubMed and Embase, Scopus and Web of Sciences. The search strategy included the keywords 'prostate cancer', 'epidemiology', 'incidence', 'mortality', 'risk factor', 'survival', 'Iran', and 'worldwide'. The search strategy was adjusted according to different requirements for each database. The specific search was also performed in cancer-related websites for Iran related information.

The incidence and mortality of PCa worldwide and in Iran

The incidence rate of PCa varies by more than 25-fold worldwide; the highest rates were estimated in Northern and Western European countries such as Norway and France[10] and in Australia/New Zealand and Northern America[11] (ASR of 111.6 and 97.2 per 100,000, respectively). Incidence rates are also relatively high in certain less developed regions such as the Caribbean (79.8), Southern Africa (61.8)[12] and South America (60.1), and the lowest rates are in Central and Eastern European countries such as Albania[13] and Republic of Moldova[10] and also in Asian populations[14] with estimated rates of 10.5 and 4.5 in Eastern and South-Central Asia[1]. With an estimated number of 307,000 deaths in 2012, PCa is the sixth leading cause of death from cancers in men worldwide (6.6% of total men deaths). Since PSA testing is more effective on incidence than mortality[15], there are less variations in mortality rates than incidence worldwide (ten-fold from approximately 3 to 30 numbers per 100,000 people) as the number of prostate cancer deaths are higher in less developed regions compared to more developed (165,000 and 142,000 numbers, respectively).

Mortality rates are generally high in predominantly black populations (Caribbean, 29 per 100,000 people and in Sub-Saharan Africa, ASRs are 19-24 per 100,000 people), they are very low in Asia (for instance 2.9 per 100,000 people in South-Central Asia) and are intermediate in the America and Oceania[1].

PCa is the sixth most common cancer and as the study of Pakzad et al[16] reported, PCa is the sixth leading cause of death from cancer in Iran, with an estimated number of 4,111 new cases and 2,297 deaths in 2012[17]. A study conducted in Iran during a 6-year period (2003-2008) showed that 9-7% of all cancers in Iranian men were PCa. In total, in the six-year study, 16,071 cases of PCa were recorded[4]. Different conducted studies in Iran showed that more PCa cases occur after 50 years of age and PCa is mostly frequent in ages of 70-79 years old[18-21], which is related to the morphology of adenocarcinoma. Pakzad et al[17] also reported that the most common morphology (adenocarcinoma) decreased from 97.61% in 2003 to 90.97% in 2008; this reduction was significant with an APC of -3.3 (CI: -7.4 to 0.9)[4]. Compared to the Western countries like the United States, Iran has a remarkable lower incidence rate of PCa[22]. This large disparity in the incidence of PCa may be due to a combination of genetic, environmental factors, diet, lifestyle, widespread clinical examinations, and most importantly access to preventive and diagnostic services like PSA testing in developed countries[23-25].

The incidence of PCa is also affected by geographical region in Iran[4]. Few studies have been conducted on the epidemiology of PCa in Iran[5]. The results of Sadjadi et al[23] (based on Iran Ministry of Health Guidelines) showed that there were evident regional differences in the incidence of PCa in Iran. The results of the first report of cancer incidence in Tehran at 2009[26], showed that after stomach cancer, PCa is the second most common cancer among men in Teheran, with an ASR of 15.6. According to the results of another report[23]

which has been based on obtained data from Cancer Registries (which covered five provinces during the five years of study period (1996 to 2000), the ASR of this cancer was calculated as 5.1 and there were no statistically significant differences in ASR of PCa among these five provinces per 100,000 people-years (p>0.05). Mousavi[27] showed that the ASR was 9.41 during 2005-2006 years.

Major Risk factors of PCa

Drinking and Smoking

In terms of diet and nutrition, some studies have found a significant association between smoking and beverage consumption[28,29]. Findings of meta-analysis studies of Fillmore et al[29], Rota et al[30] and Zhao et al[3], showed a significant relationship between high consumption of alcoholic beverages and PCa incidence. In terms of tobacco consumption, the findings of a meta-analysis study indicated that the incidence and mortality associated with PCa have increased significantly with the increase in tobacco use[31]. Various studies have provided various mechanisms about the development of tumors and morbidity caused by smoking[31,32]. For example, researchers have found that smoking increases the serum estrogen metabolism and subsequently promotes a more aggressive tumor phenotype, resulting in increased PCA-related deaths[32].

Lack of fresh fruit and vegetables

Several studies have shown that a diet containing certain vegetables (including tomatoes, cruciferous vegetables, soy beans, and other legumes) or fruit juices (such as pomegranate) is associated with lower incidence of PCa[33]. In this regard, results of a systematic study[35] showed that there is a significant association between receiving tomato-rich vegetables and tomato-rich products with reduced PCa incidence. Some case-control studies also indicated that the risk of PCa in people who intake cruciferous is significantly lower than others[36,37].

Geography

Geographically, the most commonly affected regions of PCa include North America, Australia, New Zealand, and Western and Northern Europe. The highest PCa mortality rate is estimated in low and middle-income regions, including sub-tropical Africa, South America, and the Caribbean. However, the PCa mortality rate in Asia, Africa and Central America is lower than other parts of the world[1]. The exact causes of this difference are not known, but one of the possible causes of this difference can be the advance in diagnostic methods and difference in lifestyle. For example, the risk of PCa among Asian-Americans is lower than white Americans. Also, due to the higher life expectancy in developed countries, the incidence of PCa in these countries has often increased with age[11].

Family history

PCa diagnosis in a family member is called family PCa. The prevalence rate of family PCA is estimated to be around 20%. The presence of similar genes, similar lifestyle, and similar environmental conditions are among the reasons associated with family PCa. Ventimiglia et al[38] findings showed that PCA risk is 2.3 times higher in the first-degree family members than in others. A national study also found that the chance of having a PCA in men over the age of 75 with family history of PCa was 30-60%[39]. The rate of inherited PCa is about 5% of all cases of PCa. Inherited PCa occurs when a gene mutation is transmitted from one generation to the next. Inherited PCA occurs in men who have one of the following characteristics: at least 3 of their first-degree relatives are affected by PCa; three generations of a family or two generations or more of close relatives (such as father, brother, son, grandfather, uncle, niece, and nephew) are affected by PCa[40].

Genetic changes

Documentation and knowledge about genetic contribution to PCa risks are increasing. Several genes and chromosomal regions have been found to be associated with PCa in various linkage analyses[41], case-control studies[42], genome-wide association studies (GWAS)[43], and admixture mapping studies[44]. Pathogenic variants in genes of high and moderate penetrance, such as BRCA1, BRCA2, the mismatch repair genes, and HOXB13 confer modest to high lifetime risk of PCa. The TMPRSS2 gene is prostate specific, and is expressed in both benign and malignant prostatic epithelium. TMPRSS2 expression has been showed to be induced by androgens in hormone-responsive PCa cell lines. Therefore, it is hypothesized that TMPRSS2 drives ETS gene over expression in PCa positive for TMPRSS2-ETS gene fusions[45].

Race/ethnicity

Highest PCa incidence rates were observed in African-American Caribbean men. The mortality rate from PCa among African-American men is about double than of white men. The occurrence of PCa in Asian-American and Hispanic/Latino men was lower compared to non-Hispanic white men[11].

Occupation

Several studies have been carried out on occupational risk factors. The findings of a case-control study in 2016 showed that the PCA risk among forestry workers, police officers, administrative and clerical workers, white-collar occupations, and industries, such as public service, was lower compared to other occupations[46]. A study conducted in 2013 also suggested that the risk of PCA in farmers is 4 times higher than others[47]. One of the reasons why PCa is higher in farmers is farmer's exposure to pesticides[46]. Parent et al[48] also found that the exposure to various chemicals such as pesticides, acetic acid, arsenic compounds, polycyclic aromatic, gasoline and diesel engine emissions, mono-nuclear aromatic hydrocarbons, lubricating oils has significantly increased the risk for PCA. This study also found that the risk of PCa is generally twice in farmers using pesticides than others[48]. Other study findings also indicate that PCA risk is 6 times higher for farmers exposed to diesel engine exhaust[49]. The results of a case-control study in Taiwan (2016) showed that the risk of PCa among hairdressers using hair dye was significantly higher than other hairdressers[50]. In fact, hair dye products contain over 5,000 mutagenic and carcinogenic chemicals[51-53].

Factors with less clear effect on PCa risk

Excessive use of micronutrient

Many studies recommend that use of vitamins, supplements, and specific foods are frequently reported among PCa patients[54]. A Swedish study in 2010, showed that, overall, participants with PCa were more likely to have used supplements than healthy population-based control subjects[55]. In a Canadian study, complementary and alternative medicine (CAM) use was reported among 39% of recently diagnosed PCa patients, and the most commonly used forms of CAM were herbals, vitamins, and minerals. Within those categories, saw palmetto, vitamin E, and selenium were the most popular ones[56].

Vitamin D (1, 25 dihydroxyvitamin D_3) also, is an essential vitamin that is from the super family of the steroid hormones. Human sources include both dietary intake and conversion from an inactive to active vitamin D in the skin through sunlight exposure. Interest in vitamin D as a determinant of PCa risk, comes from several epidemiologic studies that suggest[57, 58] PCa occurs more frequently in older men, with more common vitamin D deficiency. Also, a dietary intake of dairy products rich in calcium, which depresses the serum levels of vitamin D, is associated with a higher risk of PCa. Although, many studies show no association or a weak association between vitamin D levels and PCa risk[59,60]. The Cancer Prevention Study II Nutrition Cohort, a prospective cohort of 65,321 men, demonstrated a modestly increased (relative risk) RR of 1.2 for total calcium intake (dietary and supplements) and 1.6 for just high dietary calcium intake (≥2000 *vs*. <700 mg/day), but not for dairy intake. The results demonstrate that very high calcium intake, more than daily recommendation, may modestly increase cancer risks[61]. These conflicting results regarding vitamin D, calcium, and PCa risk, may be explained by variants in the vitamin D receptor (VDR). Polymorphisms resulting in a VDR with lower activity have been related to increased risk of PCa, as well as increased risk of biochemical recurrence following radical prostatectomy[62].

Estrogens

In contrast to the early study about estrogen that has been considered as protective factor against PCa and has been used as a treatment for advanced disease, evidence suggests that estrogens may play a significant role in predisposing or even cause PCa[63,64]. There is correlative evidence in humans, which indicates the effect of estrogen on the prostate gland being conducive to cancer onset. Although, blood circulating estrogen levels may not correlate well with intraprostatic levels, particularly in light of recent evidence about the intraprostatic estrogen production, serum values offer an easily accessible surrogate marker to investigate associations between estrogen and PCa risk[65]. Cussenet et al[66] found that an association was identified between polymorphisms in genes related to estrogen metabolism (CYP1B1 and CYP19) and PCa risk. There is also an increasing evidence in animal studies that estrogens may act as procarcinogens in the prostate[67]. There is evidence across multiple species that estrogens acting through stromal estrogen receptor (ER) α may contribute to prostate carcinogenesis and cancer[68]. However, the data on serum estrogen levels and PCa

risk are conflicting[69]. Complicating interpretation of serum measurements is the fact that estradiol can be produced from testosterone by intraprostatic aromatase[63]. Therefore, future research is needed in order to reach confirmation on estrogen's role in development and progression of PCa.

Obesity

There are contradictory results about the risk of obesity. Several studies have found that, despite the lower incidence of low-risk diseases in obese men, the risk of PCa in these individuals is higher than others[70,71]. The reason for this finding is not clear. Some other studies also indicated that PCa-related risk and mortality rates in obese men were significantly higher than others. However, all surveys are not consistent with this finding[74]. So, further studies are needed.

Prostatitis

Some studies have found that there was a significant association between prostatitis and PCa[75,76]. However, some other studies did not confirm this finding[77]. Cohort study findings in California (2010) also indicated that PCa risk increased in people with prostatitis [(RR) = 1.30; 95%, CI: 1.10-1.54][78]. There is a lot of evidence of long-term affliction to asymptomatic inflammatory prostatitis caused by infectious microorganisms and PCa. One of the organisms associated with PPH and PCa is the infection with *E. coli bacteria*[79, 80]. Other studies also indicated that the protozoan T. vaginalis infection caused by sexually transmitted diseases (STIs) was associated with prostatitis and PCa[81]. In general, the association between prostatitis and PCa has not been definitely demonstrated, and further studies are needed in this field.

Vasectomy

Existence of a relationship between vasectomy and PCa risk was initially suggested in 1993 with a RR of 1.6 based on two large cohort studies[82,83]. The risk increased by aging, so that men who underwent vasectomy at an early age, had a lower risk. A recent meta-analysis reported a pooled RR of 1.37, with a linear trend suggesting a 10% increase for each additional 10 years since vasectomy[84]. On the other hand, a meta-analysis of cohort studies suggested that vasectomy was not associated with increased risk of PCa[85]. Therefore, research on this possible association is still under way.

Sexual Activity/Sexually Transmitted Diseases

Some studies have found that there is a significant relationship between the incidence of STIs and the incidence of PCa[81,86,87]. It is assumed that sexual behavior and associated exposure to infectious agents increases the risk of PCa[87]. Meta-analysis study findings also confirmed a significant relationship between PCa and STI (odds ratio [OR] = 1.48, 95% CI = 1.26 to 1.73), gonorrhea (OR = 1.35, 95% CI = 1.05 to 1.83) and human papillomavirus (OR = 1.39, 95% CI = 1.12 to 2.06)[88]. Some other studies also show a significant relationship between ejaculation frequency and PCa, so that ejaculation is a protective factor in prevention of PCa[89,90]. Findings by Doolan et al (2014)[53] also indicated that men who ejaculated more than 5 times a week had a lower risk of developing PCa. Leitzmann et al[90] found in a Cohort study that more than 21 ejaculations per week decrease the risk of developing PCa. The causes and mechanism of the protective effect of ejaculation are still unknown.

Survival

Most cases of PCa develop in older men. In many cases the cancer is slow growing and non-invasive. Therefore, it has a lower risk and only one out of 36 cases died from PCa. Likewise, most people with PCa die for different causes than PCa, such as stroke and cardiovascular diseases. The five-year relative survival rate is 100% in the local stage and 28% in the regional stage[49]. The American Cancer Society has also estimated the PCA's 10-year survival rate to be 91%. The PCA survival rate in developing countries is lower compared to developed countries due to delayed diagnosis and lack of adequate health care access[91].

CONCLUSIONS

PCa is characterized by wide variations in incidence and mortality all over the world, combined with evidence of increasing load of incidence in several areas. The rates are in the highest amounts in Australia/New Zealand and Northern America and in Western and Northern Europe but remain low in Asian populations. Compared to the Western countries like the United States, Iran has a remarkably lower incidence rate of PCa. This large disparity in the incidence of PCa may be due to a combination of genetic, environmental factors, diet, lifestyle, widespread clinical examinations, and most importantly, access to

preventive and diagnostic services such as PSA testing in developed countries. These studies may provide considerable evidence for major and minor risk factors, which may be helpful in identifying subsets of the population which are more predisposing in developing PCa. This will lead to the use of effective preventive actions, such as health education, nutritional intervention, and screening, especially in high-risk areas in the world. Furthermore, a screening program for PCa by PSA testing is highly recommended in order to discover latent asymptomatic PCa cases and to clarify the real burden of the disease, especially in developing countries such as Iran. In addition, future investigations are needed to improve our knowledge about unclear risk factors of PCa, which have been mentioned in this article.

REFERENCES

1. Cancer IAf Ro. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. 2012.
2. Facchini G, Perri F, Misso G, D Aniello C, Scarpati G, Rossetti S, Pepa CD, Pisconti S, Unteregger G, Cossu A, Caraglia M, Berretta M, Cavaliere C. Optimal management of prostate cancer based on its natural clinical history. Curr Cancer Drug Targets 2017; 28: 1-16.
3. Zhao J, Stockwell T, Roemer A, Chikritzhs T. Is alcohol consumption a risk factor for prostate cancer? A systematic review and meta-analysis. BMC Cancer 2016; 16: 1-13.
4. Pakzad R, Rafiemanesh H, Ghoncheh M, Sarmad A, Salehiniya H, Hosseini S, Sepehri Z, Afshari-Moghadam A. Prostate cancer in Iran: trends in incidence and morphological and epidemiological characteristics. Asian Pac J Cancer Prev 2016; 17: 839-843.
5. Radmard AR. Five common cancers in Iran. Arch Iran Med 2010; 13: 143-146.
6. Mousavii SM, Gouya MM, Ramazani R, Davanlou M, Hajsadegi N, Seddighi Z. Cancer incidence and mortality in Iran. Ann Oncol 2008; 20: 556-562.
7. Hosseini S, Danesh A, Parvin M, Basiri A, Javadzadeh T, Safarinejad M, Nahabedian A. Incidental prostatic adenocarcinoma in patients with PSA less than 4 ng/mL undergoing radical cystoprostatectomy for bladder cancer in Iranian men. International Braz J Urol 2007; 33: 167-175.
8. Autorino R, Di Lorenzo G, Damiano R, Giannarini G, De Sio M, Cheng L, Montironi R. Pathology of the prostate in radical cystectomy specimens: a critical review. Surg Oncol 2009; 18: 73-84.
9. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136: 359-386.
10. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh J, Comber H, Forman D, Bray F. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013; 49: 1374-1403.
11. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, Bray F. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012; 61: 1079-1092.
12. Rebbeck TR, Devesa SS, Chang B-L, Bunker CH, Cheng I, Cooney K, Eeles R, Fernandez P, Giri VN, Gueye SM, Haiman CA, Henderson BE, Heyns CF, Hu JJ, Ingles SA, Isaacs W, Jalloh M, John EM, Kibel AS, Kidd LR, Layne P, Leach RJ, Neslund-Dudas C, Okobia MN, Ostrander EA, Park JY, Patrick AL, Phelan CM, Ragin C, Roberts RA, Rybicki BA, Stanford JL, Strom S, Thompson IM, Witte J, Xu J, Yeboah E, Hsing AW, Zeigler-Johnson CM. Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of African descent. Prostate Cancer 2013; 10: 1-12.
13. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol Res 2006; 24: 2137-2150.
14. Kim C-S, Lee JY, Chung BH, Kim W-J, Fai NC, Hakim L, Umbas R, Ong TA, Lim J, Letran JL, Chiong E, Wu TL, Lojanapiwat B, Türkeri L, Murphy DG, Gardiner RA, Moretti K, Cooperberg M, Carroll P, Mun SK, Hinotsu S, Hirao Y, Ozono S, Horie S, Onozawa M, Kitagawa Y, Kitamura T, Namiki M, Akaza H. Report of the Second Asian Prostate Cancer (A-CaP) Study Meeting. Prostate Int 2017; 5: 95-103.
15. Jung KW, Won YJ, Kong HJ, Oh CM, Cho H, Lee DH, Lee KH. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2012. Cancer Res Treat 2015; 47: 127-141.
16. Almasi Z, Mohammadian-Hafshejani A, Salehiniya H. Incidence, mortality, and epidemiological aspects of cancers in Iran; differences with the world data. J BUON 2016; 21: 994-1004.
17. Pakzad R, Mohammadian-Hafshejani A, Ghoncheh M, Pakzad I, Salehiniya H. The incidence and mortality of prostate cancer and its relationship with development in Asia. Prostate Int 2015; 3 :135-140.
18. Haghighi Fatemah HA. Epidemiological retrospective study of neoplasms of prostate gland in Birjand. J Birjand Univ Med Sci 2005; 12: 9-15.
19. Farahmand M, Almasi-Hashiani A, Mehrabani D. The epidemiologic study of prostate cancer in Fars province, Southern Iran (2003-2008). J Arak Med Univ 2013; 15: 54-60.
20. Amoori N, Mirzaei M, Cheraghi M. Incidence of cancers in Kuzestan province of Iran: trend from 2004 to 2008. Asian Pac J Cancer Prev 2014; 15: 8345-8359.
21. Basiri A, Shakhssalim N, Jalaly NY, Miri HH, Partovipour E, Panahi MH. Difference in the incidences of the most prevalent urologic cancers from 2003 to 2009 in Iran. Asian Pac J Cancer Prev 2014; 15: 1459-1463.
22. Sfanos KS, De Marzo AM. Prostate cancer and inflammation: the evidence. Histopathology 2012; 60: 199-215.
23. Sadjadi A, Nooraie M, Ghorbani A, Alimohammadian M, Zahedi M-J, Darvish-Moghadam S, Fakheri H, Babai M, Semnani S, Mansour-Ghanaei F, Mohagheghi MA. The incidence of prostate cancer in Iran: results of a population-based cancer registry. Arch Iran Med 2007; 10: 481-485.
24. Hassanipour-Azgomi S, Mohammadian-Hafshejani A, Ghoncheh M, Towhidi F, Jamehshorani S, Salehiniya H. Incidence and mortality of prostate cancer and their relationship with the Human Development Index worldwide. Prostate Int 2016; 4: 118-124.
25. Facchini G, Caffo O, Ortega C, D'Aniello C, Di Napoli M, Cecere SC, Pepa CD, Maines F, Ruatta F, Iovane G, Pisconti S, Montella M, Berretta M, Pignata S, Cavaliere C. Very early PSA response to abiraterone in mCRPC patients: a novel prognostic factor predicting overall survival. Front Pharmacol 2016; 7: 1-8.

26. Mohagheghi M-A, Mosavi-Jarrahi A, Malekzadeh R, Parkin M. Cancer incidence in tehran metropolis: the first report from the tehran population-based cancer registry. Arch Iran Med 2009; 12: 15-23.
27. Mousavi SM. Toward prostate cancer early detection in Iran. Asian Pac J Cancer Prev 2009; 10: 413-418.
28. Who J, Consultation FE. Diet, nutrition and the prevention of chronic diseases. World Health Organ Tech Rep Ser 2003; 916: 1-8.
29. Middleton Fillmore K, Chikritzhs T, Stockwell T, Bostrom A, Pascal R. Alcohol use and prostate cancer: a meta-analysis. Mol Nutr Food Res 2009; 53: 240-255.
30. Rota M, Scotti L, Turati F, Tramacere I, Islami F, Bellocco R, Negri E, Corrao G, Boffetta P, La Vecchia C, Bagnardi V. Alcohol consumption and prostate cancer risk: a meta-analysis of the dose-risk relation. Eur J Cancer Prev 2012; 21: 350-359.
31. Huncharek M, Haddock KS, Reid R, Kupelnick B. Smoking as a risk factor for prostate cancer: a meta-analysis of 24 prospective cohort studies. Am J Public Health 2010; 100: 693-701.
32. Rohrmann S, Genkinger JM, Burke A, Helzlsouer KJ, Comstock GW, Alberg AJ, Platz EA. Smoking and risk of fatal prostate cancer in a prospective US study. Urol 2007; 69: 721-725.
33. Pantuck AJ, Leppert JT, Zomorodian N, Aronson W, Hong J, Barnard RJ, Seeram N, Liker H, Wang H, Elashoff R, Heber D, Aviram M, Ignarro L, Belldegrun A. Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer. Clin Cancer Res 2006; 12: 4018-4026.
34. Paller C, Ye X, Wozniak P, Gillespie B, Sieber P, Greengold R, Stockton BR, Hertzman MD, Efros R, Roper H, Liker R, Carducci MA. A randomized phase II study of pomegranate extract for men with rising PSA following initial therapy for localized prostate cancer. Prostate Cancer Prostatic Dis 2013; 16: 50-55.
35. Jinyao C, Yang S, Zhang L. Lycopene/tomato consumption and the risk of prostate cancer: a systematic review and meta-analysis of prospective studies. Prostate Cancer Prostatic Dis 2013; 59: 213-223.
36. Kolonel LN, Hankin JH, Whittemore AS, Wu AH, Gallagher RP, Wilkens LR, John EM, Howe GR, Dreon DM, West DW, Paffenbarger RS. Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Cancer Epidemiol Biomarkers Prev 2000; 9: 795-804.
37. Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. Nutr Cancer 1999; 34: 173-184.
38. Ventimiglia E, Salonia A, Briganti A, Montorsi F. Re: family history and probability of prostate cancer, differentiated by risk category-a nationwide population-based study. Eur Urol 2017; 71: 143-144.
39. Bratt O, Drevin L, Akre O, Garmo H, Stattin P. Family history and probability of prostate cancer, differentiated by risk category: a nationwide population-based study. J Natl Cancer Inst 2016; 108: 1-10.
40. Lee SH, Park KK, Chung MS, Chung BH. Clinical features of familial or hereditary prostate cancer in korean men: a pilot study. Korean J Urol 2011; 52: 9-12.
41. Stanford JL, McDonnell SK, Friedrichsen DM, Carlson EE, Kolb S, Deutsch K, Janer M, Hood L, Ostrander EA, Schaid DJ. Prostate cancer and genetic susceptibility: a genome scan incorporating disease aggressiveness. Prostate 2006; 66: 317-325.
42. Tang H, Quertermous T, Rodriguez B, Kardia SL, Zhu X, Brown A, Pankow J, Province MA, Hunt S, Boerwinkle E, Schork N, Risch N. Genetic structure, self-identified race/ethnicity, and confounding in case-control association studies. Am J Med Genet 2005; 76: 268-275.
43. Thorisson GA, Smith AV, Krishnan L, Stein LD. The international HapMap project web site. Genome Res 2005; 15: 1592-1593.
44. McKeigue PM. Prospects for admixture mapping of complex traits. Am J Med Genet 2005; 76: 1-7.
45. Abouassaly R, Thompson I, Platz EA, Klein EA. Epidemiology, etiology, and prevention of prostate cancer. Urol 2012; 10: 2704-2725.
46. Sauvé J-F, Lavoué J, Parent M-É. Occupation, industry, and the risk of prostate cancer: a case-control study in Montréal, Canada. Environ Health 2016; 15: 1-19.
47. Ragin C, Davis-Reyes B, Tadesse H, Daniels D, Bunker CH, Jackson M, Ferguson TS, Patrick AL, Tulloch-Reid MK, Taioli E. Farming, reported pesticide use, and prostate cancer. Am J Mens Health 2013; 7: 102-109.
48. Parent M, Désy M, Siemiatycki J. Does exposure to agricultural chemicals increase the risk of prostate cancer among farmers. Mcgill J Med 2009; 12: 70-77.
49. Bashir MN. Epidemiology of prostate cancer. Asian Pac J Cancer Prev 2015; 16: 5137-5141.
50. Tai S-Y, Hsieh H-M, Huang S-P, Wu M-T. Hair dye use, regular exercise, and the risk and prognosis of prostate cancer: multicenter case-control and case-only studies. BMC cancer 2016; 16: 1-12.
51. Ames BN, Kammen H, Yamasaki E. Hair dyes are mutagenic: identification of a variety of mutagenic ingredients. Proc Natl Sci Acad B Biol Sci 1975; 72: 2423-2427.
52. Czene K, Tiikkaja S, Hemminki K. Cancer risks in hairdressers: assessment of carcinogenicity of hair dyes and gels. Int J Cancer 2003; 105: 108-112.
53. Doolan G, Benke G, Giles G. An update on occupation and prostate cancer. Asian Pac J Cancer Prev 2014; 15: 501-516.
54. McDermott CL, Blough DK, Fedorenko CR, Arora NK, Zeliadt SB, Fairweather ME, Oakley-Girvan I, Van Den Eeden SK, Ramsey SD. Complementary and alternative medicine use among newly diagnosed prostate cancer patients. Support Care Cancer 2012; 20: 65-73.
55. Westerlund A, Steineck G, Bälter K, Stattin P, Grönberg H, Hedelin M. Dietary supplement use patterns in men with prostate cancer: the Cancer Prostate Sweden study. Ann Oncol 2010; 22: 967-972.
56. Eng J, Ramsum D, Verhoef M, Guns E, Davison J, Gallagher R. A population-based survey of complementary and alternative medicine use in men recently diagnosed with prostate cancer. Integr Cancer Ther 2003; 2: 212-226.
57. Stewart LV, Weigel NL. Vitamin D and prostate cancer. Exp Biol Med 2004; 229: 277-284.
58. Klein EA, Thompson IM, Tangen CM, Crowley JJ, Lucia MS, Goodman PJ, Minasian LM, Ford LG, Parnes HL, Gaziano JM, Karp DD, Lieber MM, Walther PJ, Klotz L, Parsons JK, Chin JL, Darke AK, Lippman SM, Goodman GE, Meyskens FL Jr, Baker LH. Vitamin E and the risk of prostate cancer: the selenium and vitamin e cancer prevention trial. JAMA 2011; 306: 1549-1556.
59. Chan JM, Giovannucci EL. Dairy products, calcium, and vitamin D and risk of prostate cancer. Epidemiol Rev 2001; 23: 87-92.
60. Brändstedt J, Almquist M, Manjer J, Malm J. Vitamin D, PTH, and calcium and the risk of prostate cancer: a prospective nested case–control study. Cancer Causes Control 2012; 23: 1377-1385.

61. Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Fakhrabadi-Shokoohi D, Giovannucci EL, Thun MJ, Calle EE. Calcium, dairy products, and risk of prostate cancer in a prospective cohort of United States men. Cancer Epidemiol Biomarkers Prev 2003; 12: 597-603.
62. Krishnan AV, Trump DL, Johnson CS, Feldman D. The role of vitamin D in cancer prevention and treatment. Endocrinol Metab Clin North Am 2010; 39: 401-418.
63. Nelles JL, Hu W-Y, Prins GS. Estrogen action and prostate cancer. Expert Rev Endocrinol Metab 2011; 6: 437-451.
64. Stampfer MJ, Colditz GA, Willett WC, Manson JE, Rosner B, Speizer FE, Hennekens CH. Postmenopausal estrogen therapy and cardiovascular disease: ten-year follow-up from the Nurses' Health Study. N Engl J Med 1991; 325: 756-762.
65. Barrett-Connor E, Garland C, McPhillips JB, Khaw K-T, Wingard DL. A prospective, population-based study of androstenedione, estrogens, and prostatic cancer. Cancer Res 1990; 50: 169-173.
66. Cussenot O, Azzouzi AR, Nicolaiew N, Fromont G, Mangin P, Cormier L, Fournier G, Valeri A, Larre S, Thibault F, Giordanella JP, Pouchard M, Zheng Y, Hamdy FC, Cox A, Cancel-Tassin G. Combination of polymorphisms from genes related to estrogen metabolism and risk of prostate cancers: the hidden face of estrogens. J Clin Oncol 2007; 25: 3596-602.
67. Bosland MC. A perspective on the role of estrogen in hormone-induced prostate carcinogenesis. Cancer Lett 2013; 334: 28-33.
68. Ricke WA, McPherson SJ, Bianco JJ, Cunha GR, Wang Y, Risbridger GP. Prostatic hormonal carcinogenesis is mediated by in situ estrogen production and estrogen receptor alpha signaling. FASEB J 2008; 22: 1512-1520.
69. Gann PH, Hennekens CH, Ma J, Longcope C, Stampfer MJ. Prospective study of sex hormone levels and risk of prostate cancer. J Natl Cancer Inst 1996; 88: 1118-1126.
70. Vidal AC, Howard LE, Moreira DM, Castro-Santamaria R, Andriole GL, Freedland SJ. Obesity increases the risk for high-grade prostate cancer: results from the REDUCE study. Cancer Epidemiol Biomarkers Prev 2014; 23: 2936-2942.
71. Gong Z, Agalliu I, Lin DW, Stanford JL, Kristal AR. Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle-aged men. Cancer 2007; 109: 1192-1202.
72. Freedland S, Gerber L, Bañez LL, Moreira DM, Andriole GL, Rittmaster RS. Obesity increases the risk for high-grade prostate cancer: results from the reduce study. J Urol 2011; 185: 2936-2942.
73. Gong Z, Neuhouser ML, Goodman PJ, Albanes D, Chi C, Hsing AW, Lippman SM, Platz EA, Pollak MN, Thompson IM, Kristal AR. Obesity, diabetes, and risk of prostate cancer: results from the prostate cancer prevention trial. Cancer Epidemiol Biomarkers Prev 2006; 15: 1977-1983.
74. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. Nat Rev Cancer 2004; 4: 579-591.
75. Palapattu GS, Sutcliffe S, Bastian PJ, Platz EA, De Marzo AM, Isaacs WB, Nelson WG. Prostate carcinogenesis and inflammation: emerging insights. Carcinogenesis 2005; 26: 1170-1181.
76. De Marzo AM, Platz EA, Sutcliffe S, Xu J, Grönberg H, Drake CG, Nakai Y, Isaacs WB, Nelson WG. Inflammation in prostate carcinogenesis. Nat Rev Cancer 2007; 7: 256-269.
77. Roberts RO, Bergstralh EJ, Bass SE, Lieber MM, Jacobsen SJ. Prostatitis as a risk factor for prostate cancer. Epidemio 2004; 15: 93-99.
78. Cheng I, Witte JS, Jacobsen SJ, Haque R, Quinn VP, Quesenberry CP, Caan BJ, Van Den Eeden SK. Prostatitis, sexually transmitted diseases, and prostate cancer: the California Men's Health Study. PLoS One 2010; 5: 1-9.
79. Sfanos KS, Sauvageot J, Fedor HL, Dick JD, De Marzo AM, Isaacs WB. A molecular analysis of prokaryotic and viral DNA sequences in prostate tissue from patients with prostate cancer indicates the presence of multiple and diverse microorganisms. Prostate 2008; 68: 306-320.
80. Bergh J, Marklund I, Thellenberg-Karlsson C, Grönberg H, Elgh F, Alexeyev OA. Detection of Escherichia coli 16S RNA and cytotoxic necrotizing factor 1 gene in benign prostate hyperplasia. Eur Urol 2007; 51: 457-463.
81. Sutcliffe S. Sexually transmitted infections and risk of prostate cancer: review of historical and emerging hypotheses. Future Oncol 2010; 6: 1289-1311.
82. Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. A prospective cohort study of vasectomy and prostate cancer in US men. JAMA 1993; 269: 873-877.
83. Giovannucci E, Tosteson TD, Speizer FE, Ascherio A, Vessey MP, Colditz GA. A retrospective cohort study of vasectomy and prostate cancer in US men. JAMA 1993; 269: 878-882.
84. Dennis L, Dawson D, Resnick M. Vasectomy and the risk of prostate cancer: a meta-analysis examining vasectomy status, age at vasectomy, and time since vasectomy. Prostate Cancer Prostatic Dis 2002; 5 :1930203.
85. Zhang X-L, Yan J-J, Pan S-H, Pan J-G, Ying X-R, Zhang G-F. Vasectomy and the risk of prostate cancer: a meta-analysis of cohort studies. Int J Clin Exp Med 2015; 8: 17977-17985.
86. Caini S, Gandini S, Dudas M, Bremer V, Severi E, Gherasim A. Sexually transmitted infections and prostate cancer risk: a systematic review and meta-analysis. Cancer Epidemiol 2014; 38: 329-338.
87. Huang WY, Hayes R, Pfeiffer R, Viscidi RP, Lee FK, Wang YF, Reding D, Whitby D, Papp JR, Rabkin CS. Sexually transmissible infections and prostate cancer risk. Cancer Epidemiol Biomarkers Prev 2008; 17: 2374-2381.
88. Taylor ML, Mainous AG, Wells BJ. Prostate cancer and sexually transmitted diseases: a meta-analysis. J Fam Med 2005; 37: 506-512.
89. Giles G, Severi G, English D, McCredie M, Borland R, Boyle P, Hopper JL. Sexual factors and prostate cancer. BJU Int 2003; 92: 211-216.
90. Leitzmann MF, Platz EA, Stampfer MJ, Willett WC, Giovannucci E. Ejaculation frequency and subsequent risk of prostate cancer. JAMA 2004; 291: 1578-1586.
91. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.