

Prostate Cancer: An update on the recent advances in the diagnosis and management with special reference to Saudi Arabia

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ABSTRACT. In recent years, there has been a major change in the presentation of the Cancer of the Prostate gland (CaP) in the industrially developed countries. Currently, in those countries CaP patients present in a new early pre-clinical stage designated only recently in 1992 as stage T1c. The two main factors behind this change are: the advent of Prostatic Specific Antigen (PSA) and the increased prosperity with the associated prolonged longevity. Currently, PSA is recognised as the most sensitive tumor marker widely used for CaP initial screening and for tumor monitoring. The other factor yielded to the recently noted rise the annual prevalence rates of CaP is that the male population nowadays live to ages at which the incidence of CaP peaks. Over the past two decades, CaP has been the most frequently diagnosed cancer in the American and the second most common in European men. The rates are progressively increasing. But this is not the case for eastern countries so far, especially in Saudi Arabia. On the contrary, this article will show that this cancer is still not frequently diagnosed in Saudi Arabia, a great opportunity for us to study its natural history and plan for preventive measures. Stage T1c of the prostate is a pre-clinical biopsy diagnosed cancer based upon PSA-screening. The only part of Saudi Arabia where patients commonly present in this stage is the industrially advanced ARAMCO community. In that community only, not in the whole Eastern province, dwelling elderly men are regularly screened annually by PSA testing for prostate cancer. Most of the CaP patients in the rest of Saudi Arabia present at the other later stages of the disease.

Keywords: Prostate, Cancer, Saudi Arabia.

Introduction

This review article cannot and will not discuss all aspects of prostate cancer, some of which are the subjects of intense controversies^[1]. The details of these subjects can be found in classic sources^[2-6]. The information about prostate cancer that had been undergoing rapid changes are those directly related to the recent scientific discoveries^[1-5]. It is our intention to present the data in the form of the modern evidence based medicine, *i.e.*, based on meta-analysis and statistically driven data. Traditionally, patients present to physicians with their complaints, medical history is recorded, physical examination and investigations are carried out. A diagnosis is reached and then the diagnosed disease is treated. Treatment of cancer including CaP is usually designed according to the clinical staging^[1,2]. The statistically valid reported and confirmed clinical experiences dictate our subsequent chain of reactions in the medical field. Those are: affirming the place for screening for early detection, traditional medical practices as mentioned previously, arranging the priority of investigations, making them available to every one at risk, designing the lines of management either by observation only, medical treatment, or surgical intervention taking into consideration the associated morbidities, costs, results, short and long term benefits, prognosis, and finally looking at the possibility of taking preventive measures.

The revolution in medical thinking about CaP started when it was realized in the USA and almost in the entire western hemisphere, that CaP had become the most frequently diagnosed cancer in elderly men in the last two decades^[1-4]. CaP is the second leading cause of male cancer deaths^[5]. Since the public was made aware of the figures, many men demanded to be screened by the recently available advanced methods to rest their worries about disease affection. Subsequently, more and more CaP patients have been diagnosed. More and more clinics and hospitals visits resulted because of that. More radical surgeries were performed especially for patients with asymptomatic pre-clinical stage of the disease as a result of screening of large numbers of asymptomatic men^[4]. However, frequent studies have shown that long term survival at 1 & 15 years is the same no matter what type of treatment was used^[7-8]. There has been no evidence to confirm that the mortality rate from CaP is reduced by early detection, observation only was even recommended as a standard line of management^[1,7-8]. Subsequently, urologists became divided into two groups: one group claims that CaP is a seriously killer disease, then every step should be taken to ensure very early detection and eradication of the disease in order to cure those patients (who may be healthy asymptomatic fit men) and to save lives^[9-10]. The other group claims that no matter what we do, the death rates from CaP, as based on solid statistics, are the same but high prices were paid such as worries, morbidities, and of course undeniable economical burdens. Therefore, this aggressive attitude of the 1st group is groundless^[7-8,11-12]. In the middle of all of this, where do we in Saudi Arabia stand? Which group should we follow?

To find our way ahead, we should go back to evidence-based medicine. We should look at our own statistics. Is CaP a frequently encountered disease in Saudi Arabia?

Do we have any adequate methods for monitoring? Do we have any plans for the best suitable methods of treatment? Do we have any thoughts for prevention? This short writing will try to explore these questions and issues concerning cancer of the prostate.

Epidemiology: An extensive effort was made to trace all CaP cases that were reported from 1975-1996, with the conclusion that, in Saudi Arabia, the incidence of CaP is very low compared to the western countries. All papers and presentations concerning CaP were reviewed in detail^[13]. A subsequent report from the Eastern region supported this conclusion^[14]. The obvious main reason for this low incidence rate is that: CaP is only common in aged male population that is lacking in Saudi Arabia whose population is predominantly young^[15]. Even when ranked among other genitourinary (GU) cancers, CaP comes as second most common after bladder cancer which is the most common GU cancer seen in Saudi Arabia^[15-16]. We reported our own experience with this cancer. Although it was a series of small number of patients, but the report was successful in stimulating the interest of others in a previously locally neglected subject and in drawing the attention to the fact that 55% of the patients presented in an advanced stage of the disease^[17]. Whether the incidence will rise with aging of the male population and with more widely spread use of PSA and performing more surgeries for presumed Benign Prostatic Hypertrophy (BPH) remains to be seen^[13].

The low incidence of CaP in the elderly Saudi males was confirmed to be a fact not a myth (*i.e.*, underdiagnosed or overlooked) by examining the rate of cancer discovered in prostatic specimens removed at surgery done for a clinically presumed benign disease^[18-21]. We have determined our own rates, still lower than the western rates^[22]. When we looked at other centers in the country, they were even lower^[23-27]. See an update of these rates (Table 1). Whether these rates will change in the future due to changing the dietary habits and other environmentally related risk factors also remain to be observed. In a study to explore the relationship of CaP to the nutritional status of Saudis, the incidence rate of CaP was 3.1 per 100,000 persons in 2,270 screened Saudi males. The low incidence of this cancer was re-confirmed despite a high fat diet with 50% saturated fat content^[28].

The exact morbidity and mortality rates from this cancer on the national scale are not known in Saudi Arabia. However, there was a major effort to study hospital deaths in one hospital^[29]. The death rate from prostate cancer during 1991-1995 at Asir Central Hospital was 1.5% (4 cases) among 261 cancer deaths. Among cancer deaths CaP was in the 13th position compared to the 2nd position in the USA. This is a very low rate, although, in the epidemiological sense, this rate should be expressed as a number per 100,000 of the population per year. In Scandinavian countries whose population is known to live to advanced ages, this figure is high at a rate of 22 per 100,000 per year. The dense population in the southern area of Asir is also known to have prolonged longevity. There are two studies from the Dhahran Health Center in Saudi ARAMCO^[30-31]. In 1998, a study was presented to reveal that there were 137 CaP cases seen over the previous 10 years^[30]. This has resulted in a shift in the presentation to organ con-

finned tumor in up to 53-60% of the cases. In the following year, the second study revealed that there were 20 patients with clinically confined organ disease who underwent radical prostatectomy attempting for cure by disease eradication. Pathologically, 9 (45%) were upstaged post-operatively, 3 found to have nodal metastasis and 6 had malignancy involving the surgical margins. Out of the 11 patients with organ confined disease, 33.3% returned with recurrences. The other post-operative complications and morbidities following this major surgery were not detailed^[31].

TABLE 1. Rates of incidentally discovered carcinoma of the prostate in surgical specimens removed for clinically benign disease in Saudi Arabia.

Author	Year of Report	Center	City / Area	Incidence Rate (%)
Taha ^[23]	1993	King Faisal University	Al Khobar	1.1
Al Jasser <i>et al</i> ^[24]	1995	Security Hospital	Riyadh	4.0
Ghali <i>et al</i> ^[25]	1996	King Saud University	Asir	1.6
Mosli ^[22]	1997	King Abdulaziz University	Jeddah	7.2
Al Zahrani ^[26]	1999	King Faisal Specialist Hospital	Riyadh	3.0
Al Masry ^[27]	2000	Bin-Jalawi Hospital	Al Ahsa	2.8

Clinical Presentation: There are no specific symptoms of the early cancer of the prostate. It is either discovered incidentally or searched for by PSA screening and Digital Rectal Examination (DRE). Transrectal Ultrasonography (TRUS) and transrectal ultrasound guided needle biopsy follows if one or both tests were abnormal^[1-6]. Late stages of CaP may be present by lower urinary tract obstructive symptoms similar to those of BPH. Rarely, CaP may present by renal failure due ureteral obstruction. Symptoms of metastasis include bone pains, pathological fractures, spinal cord compression or symptoms of other organ involvement that occur rarely^[1-6].

Early detection is by screening of asymptomatic men or during the evaluation of BPH. Another situation in which CaP is discovered incidentally is after Trans-urethral Resection of the Prostate (TURP) done for a clinically presumed BPH, when the histopathological examination of the excised tissues reveals cancerous tissue. This is designated as stage T1a & T1b. Stage T1c is CaP diagnosed by needle biopsy done because of elevated serum PSA level. Currently, this latter stage is most commonly described in the American literature. Reports from the ARAMCO Health Center seem to follow the same tract because of the initiation of a PSA-based screening program for the male employees above the age of 50 years and their dependants^[30-31]. The rest of the staging system is shown in Table 2^[1-6].

A survey conducted among urologists practicing in the western region of Saudi Arabia revealed that only 47% of them would commonly use PSA for screening for CaP^[32]. A survey conducted on the national scale revealed that PSA is available to 29%

only of the Saudi Ministry of Health (MOH) hospitals and 100% of all other hospitals [33]. Therefore, MOH hospitals would not be a valid source of data in regard to PSA-based screening for prostate cancer among BPH and other patients [34]. Table 3 summarizes the clinical presentation of CaP patients in Saudi Arabia [17,30,35-37]. The rates of incidental cancer discovered after prostatectomy for a presumed clinically benign disease (stages T1 & T1b) in Saudi Arabia are detailed in Table 1. We have to wait for future reports on rates of incidental cancer discovered by PSA screening (stage T1c) in the different parts of Saudi Arabia but we suspect it will be highest in ARAMCO patients since there has been a PSA screening program initiated in 1995 and lowest in MOH patients since they have the lowest availability of PSA testing. We also suspect a general increase in the incidence of this disease with a shift towards early diagnosis at early stages because of increased awareness and improvement of health care.

TABLE 2. Clinical staging of prostate cancer^[1-2].

		Description
Incidental finding; no tumour palpable Whitmore-Jewett	TNM(1992)	
Incidental finding; no tumour palpable	T1a	Tumour found by chance in <5% of excised tissue
A1	T1b	Tumour found by chance in >5% of excised tissue
A2	T1c	Tumour confirmed by needle biopsy (raised PSA)
	Tx	Local tumour cannot be evaluated
	To	No local tumour detectable
Intracapsular palpable tumour	T2a	
B1	T2b	Tumour limited to half of one lobe or less
B2	T2c	Tumour has spread to half of one lobe but not both
B3		Tumour has spread into both lobes
Extracapsular tumour		
C1	T3a	Unilateral extracapsular spread
C2	T3b	Bilateral extracapsular spread
	T3c	Tumour has spread to one or both seminal vesicles
	T4	Tumour is attached or has invaded adjacent structures other than the seminal vesicles
Disseminated tumour		
D1	Nx	Loco-regional lymph nodes cannot be evaluated
	N0	No lymph nodes involvement
	N1	Lymph nodes <2 cm in diameter
	N2	One node only > 2 cm or < 5 cm; multiple <- 5 cm
	Mx	Distant metastasis cannot be evaluated
	M0	No distant metastasis present
	M1	Distant metastasis present
D3 tumour has become resistant to hormonal therapy		a=lymph nodes other than regional nodes b=skeletal c=other sites

Diagnostic Modalities: As mentioned previously, CaP is present in different ways and none of them is specific to the disease. On physical examination, DRE is of paramount importance. Unfortunately, DRE has been proven to be an insensitive method for CaP discovery - even when done by experts [38-39]. All urologists in the Western region replied that they are performing this examination routinely [32]. In one hospital of

our own, the examination was shown not to be done adequately in the non-urological surgical and medical services^[40]. However, abnormality of the gland suspicious of cancer can be palpated in the form of a discrete nodule, more than a nodules, firmness, hard mass or a sheath like hard area. Extracapsular penetration can also be palpated during DRE.

TABLE 3. The clinical presentation of CaP patients in Saudi Arabia.

Author	Al Otaiby ^[35]	Al Kudair ^[36]	Mosli ^[17]	Abmelha ^[37]	Al Otaiby ^[30]
Center	RAFH	KFNGH	KAUH	RAFH	ARAMCO
City/area	Riyadh	Riyadh	Jeddah	Riyadh	Dhahran
Year of Report	1995	1996	1997	1998	1998
No. of Patients	126	74	55	90	137
Study Period (yrs)	12	12	11	17	10
Prostatism	unknown	30%	65%	89%	unknown
Renal Failure	unknown	unknown	5%	unknown	unknown
Incidental	19%	36%	27%	9%	unknown
PSA-screening	unknown	unknown	4%	unknown	probably high
Localized disease	52%	50.7%	45%	35%	53-60%
Metastatic stages	48%	49.3%	55%	65%	33-47%

As mentioned previously, serum PSA measurements have been proven to be a very sensitive method to aid in the initial diagnosis, monitoring of disease progression, evaluation of treatment efficacy and finally detection of early relapse and determination of prognosis^[1-6]. There are many issues concerning PSA that cannot be discussed here because of space limitation. The best to mention is to take into consideration the amount of PSA in relation to the size of the gland (PSA density), meaning that even large benign gland can produce abundant PSA but small glands are not supposed to unless they are affected with cancer or other diseases that make the cells break down and release their intracellular PSA into the circulation. The second issue is to take the age of the patient into consideration. Age-related PSA is discussed elsewhere, defined as a specific pattern of increase in the PSA serum level with increased age^[1]. There is an increase in the size of the gland itself with aging in general^[41]. Table 4 shows the age specific PSA reference ranges^[1-6]. Measurement of the free and total PSA and calculating the free/total ratio have been shown to help in reducing the rate of performing unnecessary biopsies in situation when CaP is suspected, *i.e.*, abnormal gland on DRE, mildly elevated PSA or abnormality seen on ultrasonographic scanning of the gland^[1-6]. All these issues have not been studied in Saudi patients in specific if we believe that there might be differences in the genetic make-up that is responsible about the prevalence of CaP, size of the prostate gland, androgen dependant PSA production and finally CaP behaviour in the individual patient^[5-6,42].

Transrectal Ultrasonography (TRUS) has been shown to be the best procedure in visualizing the prostatic tumor, staging of the localized tumor, and an accurate method to

guide needle biopsy. When cancer nodule is present, it appears as a discrete hypoechoic area. However, TRUs have not been shown to be a useful method of initial screening nor is it a sensitive method when used alone in the diagnosis since about 30% of the tumors are isoechoic^[2-6]. Other standard imaging techniques, such as, plain x-rays, abdominal ultrasonography, CT scan, MRI, and nuclear bone scan are useful in the evaluation of the kidneys, liver, lymph node and bone involvement.

TABLE 4. Age specific PSA normal reference ranges.

Age (years)	PSA Level (ng/mL)
40 to 49	0 to 2.5
50 to 59	0 to 3.5
60 to 69	0 to 4.5
70 to 79	0 to 6.5

Treatment Modalities: The current method of treatment of CaP is determined according to the stage of the disease^[2-6]. The clinical staging system is mentioned in Table 2. In general, there are four methods of treatment. Continuous observation only has been recommended for the early and asymptomatic metastatic disease^[7-8]. Curative surgical intervention of the fit patient with a reasonable life expectancy means the of radical excision of the prostate gland harboring a localised cancer. This radical retropubic prostatectomy has become one of the most commonly performed operations in the USA with a concomitant fall in the rate of performing TURP for BPH. It is rarely performed in Saudi Arabia, even in the major cancer centers, such as, King Faisal Specialist hospital and Research Center (KFSH & RC). Adversely and significantly affecting the quality of life, this operation commonly results in urinary incontinence, erectile impotence and bladder neck stenosis^[2-6]. Most of the operated Saudi patients had this operation done in the USA^[17]. Twenty patients only were subjected to this operation during 1989 to 1998 at the Dhahran Health Center (DHC)^[31]. Another surgical intervention that can be used (usually for advanced stages) is the surgical removal of the testes, the source of the androgen. CaP is a hormone (androgen)-dependent tumor in its early stages and well differentiated forms. Surgical castration or bilateral orchiectomy is a simple, effective, cost-effective, and acceptable operation, especially for the very elderly, symptomatic, non-complaint or poor patients. Other surgical interventions can be used to repair pathological fractures or to decompress metastasis to the spinal canal.

Similarly, palliative radiotherapy can be used to alleviate the pain of metastatic bony lesions, vertebral column metastasis and as a trial to control local tumor recurrences following radical retropubic prostatectomy. Curative radical radiotherapy using external beam irradiation and intraprostatic radiotherapy using radioactive seeds and needles have also been in use. We have little experience with type of therapy due to the small number of patients we encounter. Medical treatment in the form of medical castration by using LH-RH analogue monthly injections to suppress the anterior pituitary gland is commonly used in Saudi Arabia and the rest of the world. It is an effective method to temporary control the advanced stages of the disease. There are several

preparations intended to act as depot with an effect lasting from 4-12 weeks post injection. Therefore, the injection is either given deep intramuscularly or a bullet administered subcutaneously. However, it is costly and requires an alert and compliant patient. All androgen suppressive therapy is expected to result in loss of libido and erectile potency. There are also oral anti-androgen preparations. The best timing for their use is at the initiation of LH-RH analogue therapy to prevent the flare up of the disease that may accompany the initial rise in the serum testosterone level from LH stimulated release before its depletion. Still, these preparations are expensive, hepatotoxic and require compliance. Unfortunately, there are no encouraging reports to indicate complete or partial responses to any of the known chemotherapeutic agents whether used alone or in combination^[2-6].

Eventually, the tumor will escape the hormonal dependant state and the host will die either because of the cancer (the cancer death) or due to another reason (non-cancer death). It is important to document in the death certificate whether the patient died with CaP apart from other reasons, *e.g.*, cardiac or from CaP itself. The majority of CaP deaths are due to metastasis^[39]. This documentation of the morbidity and mortality rate helps in strategic planning of our health policy as mentioned earlier in the article.

Discussion

This part will be devoted to discuss the various risk factors involved in the development of CaP in relation to the local environment in Saudi Arabia^[43]. The two well known risk factors for developing prostate cancer are increased aging and the presence of gonadal androgenic hormones^[2-3]. Other unestablished factors recently studied are: hereditary and familial factors, descendants of the black African-American race, high fat diet, smoking, alcohol intake, vitamin D deficiency, prior vasectomy, the increased use of TURP for BPH and finally the widespread use of PSA as a screening tool for prostate cancer^[43].

Autopsy studies performed in the USA revealed that microscopic foci of well differentiated adenocarcinoma of the prostate are highly prevalent in men over the age of 50^[3]. Subsequently, it is realized that this cancer is prevalent in aging populations and infrequent in younger populations^[1-6]. With the improvement in the general living conditions and medical care, it is expected that the age distribution will change globally towards an increase in the life expectancy^[3]. The current population in Saudi Arabia is mainly formed of younger age groups^[15]. Therefore, the low current prostate cancer detection rate is consistent with the fewer number of aged males in this country.

The presence of gonadal androgenic hormones is required for cancer prostate development and in the absence of gonadal androgens the prepubertal prostate atrophies and cancer does not develop. Androgen deprivation is a well established method to control cancer prostate^[2-6]. It has been postulated that a low fat diet consumption may lead to lower serum testosterone levels^[1]. To establish any relationship between hor-

monal levels in the different age groups and the risk of development of prostate cancer, an extensive research work is required. However, several studies have considered the Mediterranean style diet to be protective against endocrine cancer. It appears that prostate cancer results from an interplay between endogenous hormones and environmental influences that include, most prominently, dietary fat. Even the different types of fat may play a different role^[44]. Olive oil seems protective but the link of pork fat to this cancer has not been established^[45]. On the contrary, Jews who do not eat pork still had a higher incidence of cancer prostate than non-Jews living in Palestine^[44]. The current Saudi diet is rich in non-pork red meat and is not devoid of fat. It is hard to speculate the long term impact of the current dietary habits of the present predominantly young generation on the future development of prostate cancer^[28].

Black African-American men represented a particularly high risk group for the development of prostate cancer and they have the highest incidence of prostate cancer in the world^[46-51]. In this group of men and in those with positive family history, the general recommendation to undergo annual screening for prostate cancer with DRE and PSA for men above the age of 50 is modified to start at a much earlier stage^[5]. Thirteen percent of the men of our series were black^[17]. Whether the high risk of prostate cancer is limited to the African-American blacks or generalized to include other black populations in mixed racial cultures deserves to be observed. In our mixed population, the cancer registry should consider the ethnic and racial variations^[46-51].

With regard to family history, prostate cancer is believed to occur in 3 forms: (1) sporadic occurrences randomly in the population, (2) familial-the unpredictable clustering of the disease in families and (3) hereditary-early onset of disease and clustering in individual families^[52-54]. In our series, 47% of the patients were younger than 70 years of age^[17]. Members of the immediate family of some of the patients are now coming forward willing to be screened by DRE and PSA but no case of familial prostate cancer has been discovered so far. The effect of consanguinity commonly seen in Saudi marriages is to be studied in the light of this current knowledge of the hereditary aspects of prostate cancer. It is imperative that family history be carefully taken and recorded in every case for future analysis^[52-54].

Data has been presented to show that neither smoking nor alcohol consumption seriously increases the risk of prostate cancer^[55]. History of vasectomy, an operation rarely performed in this country, did not appear to influence the incidence of prostate cancer and neither did the characteristics of sex lives^[35]. An increase towards the diagnosis of early stage and incidental adenocarcinomas recovered by TURP may indicate early detection rather than elevated risk^[56]. Based on the previous discussion indicating the high prevalence of microscopic cancer with increased age, the increased rates of pathological examinations of prostatic tissues obtained by resection or biopsy in elderly men will no doubt be associated with increased "cancer detection" rates. This unestablished risk factor is anticipated in this country with the significant improvement of medical care and the increased number of both urologic surgeons trained to perform TURP and the increased number of elderly males undergoing TURP for

symptomatic BPH^[34].

Data was presented to support the hypothesis that the exposure to ultraviolet (UV) rays and abundance of vitamin D may protect against clinical prostate cancer^[57]. However, it is disappointing to know that our own studies have shown that the Saudi population is at a significant risk of vitamin D deficiency. The traditional Arabic attire and head cover may play a role in diminished exposure to UV rays^[58]. During the most sunny seasons, exposure to UV rays was found to be minimal to avoid the extreme associated heat^[59]. Vitamin D deficiency and lack of exposure to UV is an unestablished risk factor for developing prostate cancer that may be paradoxically playing a role against the low rate of prostate cancer seen in this sunny country.

Screening based on PSA identifies some men with prostate cancer who have significantly increased proportion of organ-confined tumours compared with those detected through evaluation for an abnormal DRE alone^[39,60]. A subsequent study reported that increased incidence of prostate cancer is likely a result of widespread use of PSA^[60]. However, a survey conducted in the western region of Saudi Arabia to examine the current practice in evaluating prostatic diseases revealed that 47% of the surveyed centres do not use PSA freely and that PSA was available to 29% only of the Saudi MOH hospitals^[32-33]. Therefore, the risk of widespread use of PSA to increase prostate cancer detection is probably not present at this time at least in the majority of Saudi Arabia. In other words, the low rates of prostate cancer detection is consistent with the current decreased use of PSA as a screening tool.

In conclusion, carcinoma of the prostate occurs at a low frequency rate in Saudi Arabia. This should encourage us to keep the medical care given to the small number of patients encountered at the highest possible standards. We should recognize patients at risk mainly aged male relatives of CaP patients and offer them screening. Screening of individuals descending from the black African race could also be justified. However, it appears from the data presented in this review article that screening of the general aged male population in Saudi Arabia does not seem to be justified at the present time. Uniform reporting of the different aspects of the disease would be highly welcomed for disease monitoring. We will keep monitoring this disease and welcome any collaborative work in tracking newly diagnosed cases, their mode of presentation, staging, methods of treatment, outcome and finally rates of survival. All of this input will add to our knowledge and the search for the reason of this low incidence rate may lead us to find a way to keep the incidence as low as possible or even to find effective preventive measures against cancer of the prostate, a worldwide killer disease.

References

- [1] **Stricker PD.** Prostate cancer: issues and controversies. *Mod Med Middle East* 1997; **14**: 43-54.
- [2] **Walsh PC, Retik AB, Vaughan DE, and Wein AJ.** Carcinoma of the prostate, in: *Campbell's Urol*, 7th edn., WB Saunders Company, USA 1998; (**Part XI**): 2487-2553.
- [3] **Gittes RF.** Carcinoma of the prostate. *New England J Med* 1991; **324**(4): 236-245.

- [4] **Kozlowski JM, Grayhack JT.** Carcinoma of the prostate, in: *Adult and Pediatric Urol*, 3rd ed., Edited by Gillenwater JY, Grayhack JT, Howards SS, Duckett JW, M Mosby Year Book 1996; Chapter 32.
- [5] **Kirby RS, Christmas TJ, Brawer M,** in: *Prostate Cancer*, M Mosby, London 1996.
- [6] **Rizvi SAH, Naqvi SAA.** The diagnosis and treatment of prostate cancer. *Postgrad Dr Mid East* 1997; **20(2)**: 58-64.
- [7] **Johansson JE, Adami HO, Andersson SO, Bergstrom R, Holmberg L, Krusemo UB.** High 10-year Survival rate in patients with early, untreated prostatic cancer. *JAMA* 1992; **267(16)**: 2191-2196.
- [8] **Johansson JE, Holmberg L, Johansson S, Bergstrom R, Adami HO.** Fifteen-year survival in prostate cancer: a prospective population based study in Sweden. *JAMA* 1997; **277(6)**: 467-471.
- [9] **Walsh PC.** Why make an early diagnosis of prostate cancer? *J Urol* 1992; **147**: 853-854.
- [10] **Porter AT, Zimmerman M, Ruffin M, Chernew M, Callaghan C, Davis R, Lee F, Montie J, Swanson GM, Oesterling JE.** Recommendations of the First Michigan Conference on prostate cancer. *Urology* 1996; **48(4)**: 519-534.
- [11] **Schroder FH.** Screening, early detection, and treatment of prostate cancer: a European view. *Urol* 1995; **46**: 62-70.
- [12] **Denis LJ.** Prostate cancer screening and prevention: realities and hope. *Urol* 1995; **46**: 56-61.
- [13] **Mosli HA.** Prostate cancer in Saudi Arabia: review of the literature (1975 -1996). *Ann Saudi Med* 1997; **17(5)**: 510-514.
- [14] **Al Tamimi TM, Ibrahim EM, Ibrahim AM, Al-Bar AA, Assuhaimi SA, Gaberiel GS, Mishriky AM, Al Adrissi HY, Al Sobaihani MO, Al Sibai MH.** Cancer in the Eastern Region of Saudi Arabia: a population based study (1987-1988). *Ann Saudi Med* 1997; **17(1)**: 53-65.
- [15] **Al Hamdan NA, Al Zahrani A, Harper DM, Koriech O & Bazerbashi S.** National cancer registry 1994 report, *MOH*, Kingdom of Saudi Arabia: cancer incidence in Saudi Arabia. 1996 (May): 25-26.
- [16] **Koreich OM, Al Otaiby KE, Ammar F.** Urologic and male genital cancers: the Riyadh Armed Forces Hospital Experience. Paper presented at the 7th *Saudi Urol Conf*, Riyadh, Saudi Arabia 1992, November 11-12.
- [17] **Mosli HA.** Prostate cancer: experience at King Abdulaziz University Hospital, Jeddah. *Ann Saudi Med* 1997; **17(6)**: 590-594.
- [18] **Hanash KA, Utz DC, Cook EN, Taylor WF, Titus JL.** Carcinoma of the prostate: a 15-year follow-up. *J Urol* 1972; **107(3)**: 450-453.
- [19] **Jewett HJ.** The present status of radical prostatectomy for stages A & B prostatic cancer. *Urol Clin North Am* 1975; **2(1)**: 105-122.
- [20] **Sheldon CA, Williams RD, Fraley EE.** Incidental carcinoma of the prostate: a review of the literature and critical reappraisal of classification. *J Urol* 1980; **124(5)**: 626-631.
- [21] **Smith JA, Cho YH.** Management of stage A prostate cancer. *Urol Clin North Am* 1990; **17(4)**: 769-777.
- [22] **Mosli HA.** Incidental adenocarcinoma of the prostate: frequency rate at a tertiary care hospital. *Ann Saudi Med* 1997; **17(6)**: 662-664.
- [23] **Taha SA.** Prostatectomy for patients over 80 years of age in Saudi Arabia. *Saudi Med J* 1993; **14(6)**: 536-539.
- [24] **Al Jasser A, Rifai G, Kassas H.** Screening for prostate carcinoma. Paper presented at the 9th *Saudi Urol Conf*, Jeddah, Saudi Arabia 1995, 14-15 November.
- [25] **Ghali AM, El Malik EMA, Ibrahim AIA, Murad N, Al Gizawi A.** Clinical features and surgical outcome of benign prostatic hyperplasia. *Ann Saudi Med* 1996; **16(2)**: 166-170.
- [26] **Al Zahrani A, Onura V, Al Jawini N, Al Turki M, Koko AM, Mobed A, Shepl F, Kardar A,**

- Lindsted E, Kattan S, Merdad T, Percha A, Aslam M, Hanash K.** Incidental adenocarcinoma of the prostate in Saudi Arabians undergoing prostatectomy for BPH. Paper presented at the 12th Saudi Urol Conf, Al-Hada, Saudi Arabia 1999, 23-25 February.
- [27] **Al Masry AM.** Benign prostatic hypertrophy (BPH): paper presented at the 13th Saudi Urol Conf, Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia 2000, 14-17 February.
- [28] **Hanash KA, Al Othaimen, Kattan S, Lindsted E, Al Zahrani A, Merdad T, Percha A, Kardar A, Aslam M.** Prostatic carcinoma: a nutritional disease? Conflicting data from the Kingdom of Saudi Arabia. Abstract 270. *J Urol* 1999; **161**(4): 71.
- [29] **Al Shehri MY.** Hospital deaths at Asir Central Hospital. *Saudi Med J* 1999; **20**(10): 793-796.
- [30] **Al Otaibi KM, Feehan M.** Incidence of prostate cancer in Saudi ARAMCO Institution. Paper presented at 11th Saudi Urol Conf, King Fahad Military Complex, Dhahran, Saudi Arabia 1998, 24-26 February.
- [31] **Al Otaibi KM, Ayyat F, Al Jishi M, Milad M, Taheini K, Zein T.** Radical prostatectomy for prostate cancer: 10 years experience in Saudi ARAMCO. Paper presented at 12th Saudi Urol Conf, Armed Forces Hospital, Al Hada, Saudi Arabia 1999, 23-25 February.
- [32] **Mosli HA.** Survey of urological centers and review of the current practice in the evaluation and treatment of prostatic diseases in the Kingdom of Saudi Arabia. *Saudi Med J* 1996; **17**(6): 718-724.
- [33] **Abomelha MS, Al Jasser A, Taha S, Mosli HA.** Saudi Prostate Health Council: Evaluation, diagnosis, and management of BPH in Saudi Arabia: a survey of practising urologists. Paper presented at the 11th Saudi Urol Conf, King Fahad Military Complex, Dhahran 1998 24-26 February.
- [34] **Mosli HA.** BPH - The Saudi perspective. State of the art lecture presented at the 13th Saudi Urol Conf, Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia, 2000 17 February.
- [35] **Al Otaiby KE, Al Jetaily A, Abomelha MS.** Prostate cancer-the Riyadh Armed Forces Hospital experience. Paper presented at the 9th Saudi Urol Conf, Jeddah, Saudi Arabia, 1995 14-16 November.
- [36] **Al Khudair W, Mansi M, Fatthall A.** Prostate cancer: a retrospective study. Paper presented at the 10th Saudi Urol Conf, Riyadh, Saudi Arabia, 1996 26-28 November.
- [37] **Abomelha MS, Al Shyaraba M, Orkubi S, Al Jutaili A, Said M, Al Otaibi K.** Carcinoma of the prostate: experience with 90 Saudi patients. Paper presented at the 11th Saudi Urological Conference, King Fahad Military Complex, Dhahran, Saudi Arabia, 1998 24-26 February.
- [38] **Gerber GS, Thompson IM, Thisted R, Chodak GW.** Disease-specific survival following routine prostate cancer screening by digital rectal examination. *JAMA* 1993; **269**(1): 61-64.
- [39] **Catolona WJ, Smith DS, Ratliff TL, Basler JW.** Detection of organ confined prostate cancer is increased through prostate specific antigen based screening. *JAMA* 1993; **270**(8): 948-954.
- [40] **Al Khudair W, Al Fehaily MA.** Digital Rectal Examination (DRE)-are we doing enough? Paper presented at the 11th Saudi Urol Conf, King Fahd Military Complex, Dhahran, 1998 24-26 February.
- [41] **Mosli HA, Atwa MA.** The age-related prostate gland size as measured by TRUS & TURP specimens in more than 500 patients with benign prostatic diseases seen at King Abdulaziz University Hospital in Jeddah. Paper presented at the 12th Saudi Urol Conf, Al Hada and Taif Armed Forces Hospitals Program, Al Taif, 1999 25-25 February.
- [42] **Schwab ED & Pienta J.** Identification of two genes associated with metastatic prostate cancer. Abstract 2, *J Urol* 1998; **159**(5): 1.
- [43] **Pienta KJ, Esper PS.** Risk factors for prostate cancer. *Ann Intern Med* 1993; **118**(10): 793-803,
- [44] **Bitterman WA, Farhadian H, Abu Samra C, Lerner D, Amoun H, Krapf D, Makov UE.** Environmental and nutritional factors significantly associated with cancer of the urinary tract among different ethnic groups. *Urol Clin North Am* 1991; **18**(3): 501-508.

- [45] **Morton MS, Griffiths K, Blackcock N.** The preventive role of diet in prostatic diseases. *Br J Urol* 1996; **77(4)**: 481-493.
- [46] **Mottet Auselo N, Costa P, Le Pellec L, Louis JF, Navratil H.** Cancer of the prostate. 1. *Epidemiol Prog Urol* 1995; **5(1)**: 31-37.
- [47] **Boyle P, Maisonneuve P, Napalkov P.** Geographical and temporal patterns of incidence and mortality from prostate cancer. *Urol* 1995; **46 (sup 3A)**: 47-55.
- [48] **Morton RA.** Racial differences in adenocarcinoma of the prostate in North American men. *Urol* 1994; **44(5)**: 637-645.
- [49] **Smith DS, Bullock AD, Catalona WJ, Herschman JD.** Racial differences in a prostate cancer screening study. *J Urol* 1996; **156(4)**: 1366-1369.
- [50] **Myers RE, Wolf TA, Balshem AM, Ross EA, Chodak GW.** Receptivity of African-American men to prostate cancer screening. *Urol* 1994; **43(4)**: 480-487.
- [51] **Demers RY, Swanson GM, Weiss LK, Kau TY.** Increasing incidence of cancer of the prostate. The experience of black and white men in the Detroit Metropolitan Area. *Arch Intern Med* 1994; **154(11)**: 1211-1216.
- [52] **Keetch DW, Humphery PA, Smith DS, Stahl D, Catalona WJ.** Clinical and pathological feature of hereditary prostate cancer. *J Urol* 1996; **155(6)**: 1841-1843.
- [53] **Keetch DW, Rice JP, Suarez BK, Catalona WJ.** Familial aspects of prostate cancer: a case control study. *J Urol* 1995; **154(6)**: 2100-2102.
- [54] **McLellan DL, Norman RW.** Hereditary aspects of prostate cancer. *C M A J* 1995; **153(7)**: 895-900.
- [55] **Van der Gulden JW, Verbeek AL, Kolk JJ.** Smoking and drinking habits in relation to prostate cancer. *Br J Urol* 1994; **73(4)**: 382-389.
- [56] **Levy IG, Gibbons L, Collins JP, Perkins DG, Mao Y.** Prostate cancer trends in Canada: rising incidence or increased detection? *C M A J* 1993; **149(5)**: 617-624.
- [57] **Hanchette CL, Schwartz GG.** Geographic patterns of prostate cancer mortality: Evidence for a protective effect of ultraviolet radiation. *Cancer* 1992; **70(12)**: 2861-2869.
- [58] **Sedrani SH, Al Arabi K, Abanny A, Elidrissy A.** Vitamin D status of Saudis III. Prevalence of inadequate plasma 25-hydroxyvitamin D concentrations. *Saudi Med J* 1992; **13(3)**: 214-219.
- [59] **Sedrani SH, Al Arabi K, Abanny A, Elidrissy A.** Vitamin D status of Saudis IV. Seasonal Variations. *Saudi Med J* 1992; **13(5)**: 423-429.
- [60] **Stephenson RA, Smart CR.** The fall in incidence of prostate carcinoma. On the side of a prostatic specific antigen induced peak in incidence-data from the Utah Cancer Registry. *Cancer* 1996; **77(1)**: 1342-1348.

سرطان البروستاتا: تحديث المعلومات فيما يخص التشخيص والعلاج مع إشارة خاصة للمملكة العربية السعودية

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المستخلص. هناك تغيير ملحوظ في السنوات الأخيرة في الطريقة والمرحلة التي يتم بها تشخيص سرطان البروستاتا في الدول المتقدمة صناعياً. في هذه الدول يتم تشخيص هذا المرض في مرحلة مبكرة جداً حيث يتم تشخيص المرض بأخذ عينة من غدة البروستاتا بناءً على قياس مرتفع لقياس اختبار البروستاتا النوعي في الدم. هناك سببان لهذا التغيير هما اختراع طريقة قياس اختبار البروستاتا النوعي والتقدم في العمر الملاحظ حالياً بين الناس حيث أن سرطان البروستاتا ينتشر في الرجال المسنين. صحيح أن هناك زيادة في انتشار الإصابة بمرض سرطان البروستاتا في العالم الغربي ولكن هذا لا ينطبق على المملكة العربية السعودية ما عدا محيط بيئة شركة الزيت العربية (ارامكو) حيث يطبق برنامج الاكتشاف المبكر لسرطان البروستاتا عن طريق المسح السنوي للرجال المسنين بقياس اختبار البروستاتا النوعي.