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Accuracy of the contemporary Epstein criteria to predict insignificant prostate cancer in North African Man

A. Ammani[a,b,c,*], **A. Janane**[d], **B. Bouzide**[b], **Y. Dehayni**[b], **M. Lezrek**[b], **M. Ghadouane**[d], **A. Ameur**[d], **M. Abbar**[d], **A. Qarro**[a,b], **M. Alami**[a,b]

[a] *Department of Urology, Faculty of Medicine and Pharmacy, University Sidi Mohammed Ben Abdellah, Fez, Morocco*
[b] *Department of Urology, Universitary Military Hospital Moulay Ismail, Meknes, Morocco*
[c] *Center of Doctoral Studies (PhD) of Life and Heath Sciences, Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco*
[d] *Department of Urology, Universitary Military Hospital Mohammed V, Rabat, Morocco*

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Abstract
Objective: To determine the accuracy of the contemporary Epstein criteria for predicting insignificant and organ-confined prostate cancer in a North African ethnic group of patients who were eligible for active surveillance based on these criteria, but had been subjected to radical prostatectomy.
Patients and methods: A total of 340 North African men underwent radical prostatectomy for clinically localized prostate cancer at two academic institutions between January 2006 and September 2013. In 74 of these patients (21.76%), prostate cancer had been assumed to be insignificant based on the contemporary Epstein criteria. The radical prostatectomy specimens were analyzed in order to identify the rate of pathologically unfavorable prostate cancer, defined as either pathologic Gleason score 7–10 and/or a tumor volume > 0.5 cc, and/or non-organ-confined disease (stage ≥ pT3a and/or pN1 and/or positive surgical margins).

* Corresponding author at: N0 772, Hay El menzeh, C.Y.M., 10100 Rabat, Morocco.
E-mail addresses: ammani-1@hotmail.com (A. Ammani), a.janane@yahoo.fr (A. Janane), bbouziduro@hotmail.com (B. Bouzide), dr.dehayni@gmail.com (Y. Dehayni), lezrekmohamed@gmail.com (M. Lezrek), m1_ghado@yahoo.fr (M. Ghadouane), ahmed.ameur@yahoo.fr (A. Ameur), abbar11@yahoo.fr (M. Abbar), alami.mohammed1@yahoo.fr (M. Alami).
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Results: Gleason sum upgrading (≥7) was necessary in 16 (21.6%) and upstaging of the radical prostatectomy specimens in 18 patients (24.3%). Simultaneous upstaging and upgrading of the specimens was observed in 12 patients (16%). A tumor volume ≤ 0.5 cc was found in 42 patients (57%). The rate of multifocality of prostate cancer (≥2 foci) was 59.5%. The accuracy of the contemporary Epstein criteria for predicting insignificant prostate cancer was 57%, while it predicted organ-confined disease in 85%.
Conclusion: The contemporary Epstein criteria used for the identification of clinically insignificant prostate cancer have been found to underestimate the real state of prostate cancer in as many as 43% of our patients. They were a good tool for predicting organ-confined rather than insignificant prostate cancer in our North African patients. Therefore, caution is advised when the decision on the implementation of active surveillance or focal therapy is solely based on these criteria.

Introduction

As a consequence of the widespread use of assessment of the prostate-specific antigen (PSA) and digital rectal examination (DRE) in combination with extended-core prostate biopsy strategies, there is some concern about the risk of overdiagnosis and overtreatment of some forms of prostate cancer which have a protracted natural history and pose little threat to the patients during their lifetime. Stage migration resulting from aggressive PSA screening has progressively increased the proportion of patients who fall into the "favorable-risk" category; they now account for more than half of all newly diagnosed prostate cancer (PCa) patients in western countries [1–4]. As a consequence, the concept of insignificant prostate cancer (Ins-PCa) has progressively emerged in the last two decades, and alternative treatment options for these patients such as active surveillance (AS) and organ-sparing focal therapies (FT) have been implemented. However, the major obstacle to the widespread use of these conservative therapies remains the difficulty in precisely identifying low-risk PCa patients based on their pre-treatment clinical and pathologic features only [5,6].

For the period 2010–2019 Morocco has adopted the National Plan for Prevention and Cancer Control (NPPCC). The mean goal of the NPPCC is to reduce cancer-related morbidity and mortality and to improve the patients' quality of life. However, data on PCa in Moroccan men are rare, and there is only a limited number of studies providing relevant epidemiologic and prognostic information. According to the cancer registries of the cities of Rabat (2006–2008) and Casablanca (2004–2007), PCa is the second most common malignancy in Moroccan men (10.5–15.5%) after lung cancer (19.1–22.1%) [7,8]. The age-standardized incidence rate (ASIR) and the age-standardized mortality rate (ASMR) of PCa in Morocco (18.5 per 100,000 and 12.9 per 100,000, respectively, based on GLOBOCAN 2012 data [9]), have constantly increased during the last decades and are among the highest in the Middle East and North Africa (MENA Region). In contrast to western and developed countries where nowadays the usefulness of PSA screening is being questioned, the upward trends in incidence and mortality due to PCa and the high rate of advanced disease in newly diagnosed patients in Morocco and the MENA region will inevitably result in a widespread use of PSA screening and extended-core prostate biopsy. However, in the near future, practitioners in this region of the world will also be increasingly confronted with the problem of how to manage low-risk PCa. The Epstein criteria are among the most commonly used tools to identify patients with Ins-PCa who will be eligible for AS [10].

Our aim is to determine the accuracy of the contemporary Epstein criteria in predicting Ins-PCa and organ-confined disease in a North African ethnic group of patients who were eligible to AS according to these criteria but were treated with radical prostatectomy (RP).

Subjects and methods

Patient population

In total, 340 radical prostatectomies were performed at two academic Moroccan institutions (Mohammed V Military Hospital of Rabat and Moulay Ismail Military Hospital of Meknes) between January 2006 and September 2013. Out of this group, 74 patients (21.7%) fulfilled the contemporary Epstein criteria for clinically Ins-PCa after extended 10–18 core prostate biopsy: stage T1c, PSA density ≤ 0.15, Gleason score ≤ 6, fewer than three biopsies with prostate cancer, and up to 50% of cancer involvement in any core. The data of these patients were reviewed in order to assess the rate of unfavorable PCa patterns in the prostatectomy specimens. Unfavorable pathologic characteristics were defined as a Gleason sum > 6 (7–10) and/or non-organ-confined disease and/or a tumor volume > 0.5 cc. Non-organ-confined disease included extraprostatic extension, a stage ≥ pT3a and/or lymph-node involvement and/or positive surgical margins. Ins-PCa was defined as organ-confined disease, a tumor volume ≤ 0.5 cc and a Gleason sum ≤ 6.

Clinical and pathological evaluation

The clinical stage was assigned according to the 2002 TNM staging system, and pre-treatment PSA was measured before DRE and transrectal ultrasonography (TRUS). None of the patients received neoadjuvant androgen deprivation therapy. The prostate volume was assessed using TRUS with a 7.5-MHz ultrasound probe (General Electric Healthcare, Milwaukee, USA). PSA density was calculated by dividing the PSA value by the prostate volume measured on TRUS. Biopsy cores were obtained under TRUS guidance and embedded separately in multiple containers. The biopsy and radical prostatectomy specimens were staged and graded by three experienced genitourinary pathologists (A.AB., F. G. and S. M) who used standardized protocols and reporting templates. The extent of

Table 1 Descriptive characteristics of 74 North African men who fulfilled the Epstein clinically insignificant prostate cancer criteria before RP.

Variable	Value
Total population	74
Age (yr)	
Mean ± SD (median)	63 ± 4.546 (64.1)
Range	49–76
Preoperative PSA (ng/mL)	
Mean ± SD (median)	6.7 ± 1.6749 (5.7)
Range	2.1–20
Prostate volume (cm^3)	
Mean ± SD (median)	58 ± 33.57 (63.67)
Range	25–130
PSA density	
Mean ± SD (median)	0.08 ± 0.06 (0.08)
Range	0.03–0.15
No. of cores per biopsy	
Mean ± SD (median)	13.5 ± 2.6 (12.2)
Range	10–18
No. of positive cores: No. (%)	
•1	54 (73%)
•2	20 (27%)
% of cancer/positive core	
Mean ± SD (median)	10.1 ± 8.5 (7.0)
Range	0.5–45.0
Biopsy Gleason sum: No. (%)	
• <6	5 (6.7%)
• =6	69 (93.3%)

PSA, prostate specific antigen; SD, standard deviation.

Table 2 Pathologic findings at radical prostatectomy (RP) specimen.

Variable	No. of patients (%)
Total patients	74 (100%)
Tumor volume at RP specimen	
• ≤ 0.5 cc	42 (57%)
• 0.5–1.3 cc	14 (19%)
• >1.3 cc	6 (8%)
• Not reported	12 (16%)
Tumor focality	
• Unifocal	30 (40.5%)
• ≥2 foci	44 (59.5%)
Pathological Gleason sum	
• ≤6	58 (78.3%)
• 7 (3 + 4)	13 (17.6%)
• 7 (4 + 3)	2 (2.7%)
• 8	1 (1.3%)
• 9	0
• 10	0
Gleason sum upgrading at RP specimen	16 (21.6%)
Upstaging at RP specimens	
• Total	18 (24.3%)
• Stage pT2b	5 (6.7%)
• Stage pT2c	2 (2.7%)
• Non organ confined disease	
◯ Total	11 (15%)
◯ Stage pT3a	8 (72.7%)
◯ SVI	3 (27%)
◯ LNI	1 (9%)
◯ PSM	3 (27%)
Both upstaging and upgrading at RP specimen	12 (16%)

cancer invasion on the biopsy core was calculated based on the sum of all the tumor foci, excluding benign prostate tissue. The percentage of cancer in a positive biopsy core was calculated based on the ratio of the length of the cancer foci/total core length.

Pathologically, the prostatectomy specimens were included as a whole according to the Stanford protocol. The Gleason score, number of tumor foci and tumor volume, extraprostatic extension, seminal vesicle invasion, lymph node involvement, and the status of the surgical margins were evaluated for each prostatectomy piece.

The tumor volume in the prostatectomy specimens was estimated based on the dominant tumor nodule, using the three-dimensional cuboid method described by Chen et al. [11] (tumor volume = $k(0.4) \times$ length $\times$ width $\times$ thickness).

Statistical analysis

We used the IBM SPSS statistics version 20 to perform a descriptive and categorical analysis of the data. The accuracy of the Epstein criteria in predicting insignificant or organ-confined PCa was assessed using Fisher's exact test (significance at $p < 0.05$).

Results

The descriptive characteristics of the 74 North African men who fulfilled the Epstein criteria for clinically Ins-PCa before RP are summarized in Table 1. Table 2 summarizes the pathologic findings of the prostatectomy specimens.

An upgrading of the Gleason sum was necessary in 16 patients (21.6%). The final Gleason score was 7 in 15 patients (20.3%) and 8 in one patient (1.3%). The final pathology results did not reveal a Gleason pattern of 5 in any patient. Upstaging of the prostatectomy specimens occurred in 18 patients (24.3%), while the disease remained organ-confined (stages pT2b and pT2c) in 7 patients (9.4%). Non-organ-confined disease was seen in 11 patients (15%) with a pathologic stage of pT3a in most cases (72.7%). Seminal vesicle involvement (pT3b) was seen in 3 patients; in one of them final pathology also revealed lymph node involvement. Positive surgical margins were observed in 3 patients, two with a pathological stage pT3b (seminal vesicle involvement) and one with stage pT3a disease. Simultaneous upstaging and upgrading of the prostatectomy specimens was observed in 12 patients (16%). The tumor volume in the prostatectomy specimen was ≤0.5 cc in 42 (57%), 0.5–2 cc in 14 (19%) and >2 cc in 6 patients (8%). No tumor involvement was seen in the prostatectomy specimens of 12 patients (16%). The rate of multifocality of PCa (≥2 foci) was 59.5%. The accuracy of the contemporary Epstein criteria in predicting Ins-PCa (organ-confined disease, Gleason score ≤ 6 and tumor volume ≤ 0.5 cc) was 57%. The accuracy of Epstein criteria in predicting organ-confined disease (stage < pT3a, no lymph node involvement, any tumor volume, any grade) was 85% (Table 3).

Table 3 The accuracy of the contemporary Epstein criteria to predict the presence of insignificant and organ-confined disease at RP specimen in North African man.

Fulfilled contemporary Epstein criteria*	Total	Insignificant PCa**		Organ-confined disease***	
		n (%)	*p* value	*n* (%)	*p* value
Yes	74	42 (57%)	<0.0001	63 (85%)	<0.0001
No	266	23 (8.6%)		202 (76%)	

* *Contemporary Epstein criteria*: Stage T1c, PSA density ≤ 0.15 ng/mL per gram, Gleason score ≤ 6, fewer than three positive cores, and <50% of cancer involvement in any core.
** *Insignificant PCa*: organ-confined disease, Gleason score ≤6 and tumor volume ≤ 0.5 cc.
*** *Organ-confined-disease*: Stage < pT3a, No lymphnodes invasion, No positive surgical margins, any tumor volume, any grade.

Discussion

The management of low-risk organ-confined disease, especially in the subgroup of patients with presumed Ins-PCa, remains one of the most challenging problems in modern onco-urology. Currently, there is still a lack in pre-treatment diagnostic tools that can clearly distinguish significant from insignificant PCa. The contemporary Epstein criteria for clinically Ins-PCA, initially applied in the USA to a population group mainly consisting of Caucasians (over 95%) [10,12], are among the most commonly used tools to identify patients with Ins-PCa and, thus, eligible to active surveillance (AS). In the last decades, these criteria have gained interest worldwide, and several studies have been carried out to evaluate their accuracy in predicting low-risk PCa in different ethnic groups. However, the reported accuracy varies widely: 84% in the USA [12] with lower negative predictive values in African Americans (48.4%) [13], 76% in Europe [14], 54.3% in the Middle East [15] and 69.5% in Korea [16] (Table 4). Our study of a cohort of 74 North African men shows that the Epstein criteria were accurate in predicting Ins-PCa (organ confined disease, Gleason sum ≤ 6 and tumor volume ≤ 0.5 cc) in 57% and organ-confined disease (stage < pT3a, no lymph node involvement, any tumor volume, any grade) in 85%.

Many objective factors may explain the low accuracy of the Epstein criteria for predicting Ins-PCa in North African men compared to other ethnic groups. A tumor volume threshold of <0.5 cc in prostatectomy specimens is one of the most important criteria for the definition of Ins-PC as suggested by Stamey et al. [17]. The tumor volume is of prognostic significance on univariate analysis and correlates closely with the Gleason score, stage and surgical margin status of RP specimens, but there is still a lack of evidence about its independent prognostic significance in multivariate studies [18]. In the majority of studies on Epstein criteria validation, the cancer significance was determined only by the organ-confined status and the Gleason score. The inclusion of the tumor volume would probably decrease the number of Ins-PCa in these studies and further reduce the overall accuracy of the Epstein criteria. In our study, there was no report on any form of tumor volume measurement in16% of our patients which is why they were excluded from the group of patients with assumed Ins-PCa. The exclusion of the tumor volume from the defnition of Ins-PCa would naturally increase the accuracy of the Epstein criteria in our study from 57% to 78.3%.

On the other hand, the tumor volume threshold of <0.5 cc suggested by Stamey et al. for the definition of Ins-PCa and used for the selection of the ideal candidates for AS in many protocols is being challenged by a number of authors. In a study cohort similar to that of Stamey et al., Wolters et al. [19] introduced an updated tumor volume threshold for the definition of Ins-PCa. They concluded that, in cases of organ-confined PCa without Gleason patterns 4–5, the use of a tumor volume of 1.3 cc could decrease the rate of misclassification for AS selection. Based on this threshold (<1.3 cc), the accuracy of the Epstein criteria in predicting Ins-PCa in our patients will increase by 19%. In another recent study, Lee et al. [20] found that PCa patients with a tumor volume ranging from 0.5 cc to 1.3 cc and a Gleason grade of 4/5 showed an increased risk of biochemical recurrence, even when they suffered from organ-confined disease and had a preoperative PSA level < 10 ng/mL. Moreover,

Table 4 Accuracy of the contemporary Epstein criteria to predict Ins-PCa around the world.

Characteristics	Our North African study	Middle eastern study [15]	Asian study [16]	European study[14]	North American study [12]
Fulfilled Contemporary Epstein criteria: No. (%)	74/340 (21.76%)	35/70 (50%)	131/1011 (12.95%)	366/2580 (14.18%)	237/237 (100%)
Study period	2006–2013	2000–2008	2004–2009	1994–2006	2000–2003
Postoperative Gleason sum: *N* (%)					
• ≤6	56 (75.67%)	19 (54.28%)	91 (69.46%)	278 (75.95%)	214 (90.29%)
• =7	17 (22.97%)	11 (31.42%)	40 (30.53%)	88 (24.04%)	21 (8.86%)
• >7	1 (1.35%)	5 (14.28%)	0	0	2 (0.84%)
Upgraded	16 (21.62%)	2 (5.71%)	–	2 (0.54%)	1 (0.42%)
Undergraded	0	14	40	88	23
Organ-confined	63 (85%)	28 (80%)	129 (96.9%)	336 (91.8%)	217 (91.6%)
Overall Ins-PCa	57%	54%	69.5%	76%	84%

although recent reports suggest that multiparametric magnetic resonance imaging (MP-MRI) may be more reliable for evaluating a tumor volume > 0.5 cc [21], it is difficult to predict the absence of a high Gleason grade, even with more extended biopsy protocols. As it is still unclear which clinical tumor volume threshold is the best parameter to be used for AS selection and monitoring, we did not recommend an extended tumor volume (more than 0.5 cc) to be used for the definition of Ins-PCa in our patient cohort.

The threshold of 50% cancer involvement in the biopsy cores used in the modified Epstein criteria has substituted the absence of bilateral cancer used in the original study as an indicator of insignificant cancer on biopsy. However, not infrequently, a prostate biopsy may contain two or more cancer foci separated by a stretch of intervening benign tissue. Currently, there is no consensus as to the optimal method for measuring the extent or percentage of cancer in such cases. In the original study introducing the Epstein criteria, the cancer, when discontinuous, was measured from one end to the other as opposed to the measurement of the individual separate foci of cancer excluding the benign prostate tissue in between. Although, in a multivariate analysis, Karram et al. [22] found that measuring the entire stretch of cancer foci was more predictive of stage and margins than ignoring the benign tissue in between, measuring two distinct tumor foci on a needle biopsy may provide implications about whether the criteria for Ins-PCa may be applied. Measuring the two foci of cancer as if they were one single continuous focus may increase the percentage of tumor involvement to more than 50% and, therefore, will reduce the already low proportion of men fulfilling the Epstein criteria and being eligible to AS.

In our study, the percentage of cancer involvement was estimated by excluding the benign tissue in between. Nevertheless, the accuracy of Epstein criteria in predicting Ins-PCa was among the lowest in the world. Similar to the rate reported for African-Americans [13], two scenarios may explain the high proportion of prostate cancer incorrectly classified as insignificant in our patients. The first is a high incidence of anterior zone tumors in North Africans. Anterior zone cancer is known to have fewer positive and less involved cores when using the 12-core biopsy technique. The second is the presence of small-volume high-grade tumors in the peripheral zone that are not likely to be sampled on prostate biopsy due to their small size. However, the latter hypothesis is less evident, since the rate of high-grade tumors in our study was 21.6%, mostly Gleason 3 + 4 or 4 + 3 (20.3%), but without Gleason pattern 5 at final pathology.

To overcome this problem, we believe that North African men assigned to AS based on the contemporary Epstein criteria for clinically Ins-PCa may need to be followed with a 14-core biopsy sampling the anterior zone and with MP-MRI.

Our study shows the highest incidence of Gleason upgrading in patients who fulfilled the contemporary Epstein criteria (21.62% versus 0.42–5.71% in other studies). Modifications introduced by the International Society of Urological Pathology (ISUP) Consensus Conference in 2005 on Gleason scoring have resulted in an upgrading of certain pathological features of tumors with a Gleason pattern 3–4 [23]. However, none of the validation studies on the Epstein criteria indicate which Gleason system was in use. Thus, most of these studies did not apply the criteria in a proper way, which leads to a lack of valuable validation results, regardless of the ISUP Gleason score updates. The abrupt change in the predictive value of the Gleason score and the overall significance of cancer after 2005 (Table 4) suggest that the Gleason grading system is, at least partly, responsible for discrepancies between studies.

Our results are nearly similar to those of Hekal et al. [15], who also found a decreased accuracy of the contemporary Epstein criteria in predicting Ins-PCa in a Middle Eastern population (57% vs. 54%). Comparable demographic, ethnic, economic and socio-cultural characteristics between most countries of the MENA region may suggest the presence of possible links with a high aggressiveness of prostate cancer in this area. Moreover, limited data on PCa in the MENA region have led to reports of more advanced-stage disease at diagnosis in contrast to a high incidence of low-risk organ-confined PCa in most western countries [7,8,24–26]. However, in several western studies [27–30], the incidence of PCa was low among immigrants from the MENA region, and their prognosis was significantly better than that of Caucasians and Blacks. In these studies, the incidence of prostate cancer was found to be higher in immigrants from the MENA region compared to that reported in the native populations, but it was still lower than the incidence of prostate cancer seen in other ethnic groups. The inconsistency in PCa features between immigrants from the MENA region and members of the native population may be attributed to environmental, socio-cultural and professional factors as well as to the health care systems rather than to an increased ethnic risk of developing aggressive PCa.

Multifocality of PCa has been demonstrated to be frequent, varying between 60% and 90% of all cases [31]. In our study, PCa was multifocal in 59.5% of patients who fulfilled the contemporary Epstein criteria.

The real impact of PCa multifocality on the risks of upstaging and upgrading and the long-term biochemical recurrence rate remains unclear. To date, the index tumor (as measured by its largest volume) is presumed to be the driver of prognosis in most cases of multifocal PCa. Innovations in genetics and medical imaging including 3-dimensional computed tomography (3D-CT) and MP-MRI will probably increase our ability to establish the prognosis and topographical extent of all cancer foci within a prostate, leading to more precise therapeutic decisions, especially in determining candidates eligible to minimally-invasive therapies like AS and focal therapy. [31,32].

Our study shows that the contemporary Epstein criteria are not sufficient to be used clinically for predicting insignificant (as opposed to organ-confined) PCa in North African men. Thus, we believe that there is a need to re-update these criteria by adding novel tools like novel markers and MP-MRI in order to improve their predictive value for indolent PCa and to identify patients who can be safely enrolled in an active surveillance procedure.

The present study has several limitations. First, this is a retrospective study with a relatively small number of patients from one country only, which may not be representative of the whole population of North Africa. Second, we were not able to precisely define the Gleason score for each patient. However, our pathologists confirm that at least since 2007 most patients were assessed using the 2005 ISUP Gleason system modifications. Lastly, the limited follow up in our series does not allow for an evaluation of the biochemical recurrence or prognosis after radical prostatectomy in our patients, which is the most important issue in PCa rather than the presence of unfavorable pathological features.

Conclusions

Based on future projection models, the incidence and mortality rates from prostate cancer in North Africa and the Middle East are on the rise. PSA-screening appears to be inevitable in this region in order to improve migration of the currently more advanced diseases to more low-risk organ-confined diseases, and to identify more patients who would be eligible for conservative treatment approaches such as AS and FT. The contemporary Epstein criteria, even when assessed based on extended 10–18 core prostate biopsy, may underestimate the real significance of PCa in North African patients in as many as 43%. Currently, there is an ongoing need for identifying new prognostic tools (e.g. MP-MRI, molecular markers) to improve the pre-treatment prediction of Ins-PCa. So, caution is advised when the decision for AS or focal ablative therapies is based solely on these criteria in North African men.

Author's Contributions

All the authors listed in this article have materially participated in the research and/or article preparation and they all have approved the final version of this article:

Abdelghani Ammani and Abdellatif Janane have equally participated in the study design, data collecting and analysing, article writing and correcting.

Youness Dehayni and Balla Bouzide have participated in collecting the data.

Mohammed Ghadouane, Mohammed Lezrek, Mohammed Abbar, Ahmed Ameur and Mohammed Alami have participated in the study design and in correcting the article.

Conflict of interests

The authors declare that they have no conflict of interest.

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None.

Ethical approval

The ethical committees of the Universitary Military Hospitals Mohammed V of Rabat and Moulay Ismail of Meknes has approved this non interventional study.

Consent from the patient

The ethical committee has stated that there was no need of consent from patients in the present study.

References

[1] Dong F, Reuther A, Magi-Galluzzi C, Zhou M, Kupelian PA, Klein EA. Pathological stage migration has slowed in the late PSA era. Urology 2007;70:839–42.

[2] Godtman RA, Holmberg E, Khatami A, Stranne J, Hugosson J. Outcome following active surveillance of men with screen-detected prostate cancer. Results from the Göteborg randomised population-based prostate cancer screening trial. Eur Urol 2013;63(January (1)):101–7.

[3] Hayes JH, Ollendorf DA, Pearson SD, Barry MJ, Kantoff PW, Lee PA, et al. Observation versus initial treatment for men with localized, low-risk prostate cancer: a cost-effectiveness analysis. Ann Intern Med 2013;158(June (12)):853–60.

[4] Roobol MJ, Kranse R, Bangma CH, van Leenders AG, Blijenberg BG, van Schaik RH, et al. ERSPC Rotterdam Study Group. Screening for prostate cancer: results of the Rotterdam section of the European randomized study of screening for prostate cancer. Eur Urol 2013;64(October (4)):530–9.

[5] Dall'Era MA, Albertsen PC, Bangma C, Carroll PR, Carter HB, Cooperberg MR, et al. Active surveillance for prostate cancer: a systematic review of the literature. Eur Urol 2012;62:976–83.

[6] Klotz L. Active surveillance with selective delayed intervention for favorable risk prostate cancer. Urol Oncol 2006;24:46–50.

[7] Tazi MA, Er-Raki A, Benjaafar N. Cancer incidence in Rabat, Morocco: 2006–2008. Ecancermedicalscience 2013;7:338, http://dx.doi.org/10.3332/ecancer.2013.338.

[8] Bouchbika Z, Haddad H, Benchakroun N, Eddakaoui H, Kotbi S, Megrini A, et al. Cancer incidence in Morocco: report from Casablanca registry 2005–2007. Pan Afr Med J 2013;September (16):31.

[9] International Agency for Research on Cancer. World Health Organization. GLOBOCAN 2012: estimated incidence, mortality and prevalence worldwide in 2012. All Cancers (excluding non-melanoma skin cancer). Available at: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx [Accessed 15.02.15].

[10] Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA 1994;271:368–74.

[11] Chen ME, Johnston D, Reyes AO, Soto CP, Babaian RJ, Troncoso P. A streamlined three-dimensional volume estimation method accurately classifies prostate tumors by volume. Am J Surg Pathol 2003;27(October (10)):1291–301.

[12] Bastian PJ, Mangold LA, Epstein JI, Partin AW. Characteristics of insignificant clinical T1c prostate tumors: a contemporary analysis. Cancer 2004;101(9):2001–5.

[13] Kryvenko ON, Carter HC, Trock BJ, Epstein JI. Biopsy criteria for determining appropriateness for active surveillance in the modern era. Urology 2014;83(April):869–74.

[14] Jeldres C, Suardi N, Walz J, Hutterer GC, Ahyai S, Lattouf J-B, et al. Validation of the contemporary Epstein criteria for insignificant prostate cancer in European men. Eur Urol 2008;54(6):1306–13.

[15] Hekal IA, El-Tabey NA, Nabeeh MA, El-Assmy A, Abd El-Hameed M, Nabeeh A, et al. Validation of Epstein criteria of insignificant prostate cancer in Middle East patients. Int Urol Nephrol 2010;42:667–71.

[16] Lee SE, Kim DS, Lee WK, Park HZ, Lee CJ, Doo SH, et al. Application of the Epstein criteria for prediction of clinically insignificant prostate cancer in Korean men. BJU Int 2010;105:1526–30.

[17] Stamey TA, Freiha FS, McNeal JE, Redwine EA, Whittemore AS, Schmid HP. Localized prostate cancer. Relationship of tumor volume to clinical significance for treatment of prostate cancer. Cancer 1993;71(3 Suppl):933–8.

[18] Wolters T, Roobol MJ, van Leeuwen PJ, van den Bergh RCN, Hoedemaeker RF, van Leenders GJLH, et al. Should pathologists routinely report prostate tumour volume? The prognostic value of tumour volume in prostate cancer. Eur Urol 2010;57:821–9.

[19] Wolters T, Roobol MJ, van Leeuwen PJ, van den Bergh RC, Hoedemaeker RF, van Leenders GJ, et al. A critical analysis of the tumor volume threshold for clinically insignificant prostate cancer using a data set of a randomized screening trial. J Urol 2011;185:121–5.

[20] Lee DH, Koo KC, Lee SH, Rha KH, Choi YD, Hong SJ, et al. Tumor lesion diameter on diffusion weighted magnetic resonance imaging could help predict insignificant prostate cancer in patients eligible for active surveillance: preliminary analysis. J Urol 2013;190: 1213–7.

[21] Turkbey B, Mani H, Aras O, Rastinehad AR, Shah V, Bernardo M, et al. Correlation of magnetic resonance imaging tumor volume with histopathology. J Urol 2012;188:1157–63.

[22] Karram S, Trock BJ, Netto GJ, Epstein JI. Should intervening benign tissue be included in the measurement of discontinuous foci of cancer on prostate needle biopsy? Correlation with radical prostatectomy findings. Am J Surg Pathol 2011;35(September (9)):1351–5.

[23] Montironi R, Cheng L, Lopez-Beltran A, Scarpelli M, Mazzucchelli R, Mikuz G, et al. Original Gleason system versus 2005 ISUP modified Gleason system: the importance of indicating which system is used in the patient's pathology and clinical reports. Eur Urol 2010;58:369–73.

[24] Osman E, Gomha MA, Harb A, Aldayel A, Aloraifi I, Almousa R, et al. An early-detection programme for prostate cancer in Saudi men: a call from a tertiary-care centre in the Eastern province. Arab J Urol 2014;12:187–91.

[25] Zanetti R, Tazi MA, Rosso S. New data tells us more about cancer incidence in North Africa. Eur J Cancer 2010;46(February (3)):462–6.

[26] Hamdi Cherif M, Serraino D, Mahnane A, Laouamri S, Zaidi Z, Boukharouba H, et al. Time trends of cancer incidence in Setif, Algeria, 1986–2010: an observational study. BMC Cancer 2014; 14:637.

[27] Ravery V, Dominique S, Hupertan V, Ben Rhouma S, Toublanc M, Boccon-Gibod L, et al. Prostate cancer characteristics in a multiracial community. Eur Urol 2008;53:533–9.

[28] Hemminki K, Li X, Czene K. Cancer risks in first-generation immigrants to Sweden. Int J Cancer 2002;99:218–88.

[29] Visser O, van Leeuwen FE. Cancer risk in first generation migrants in North-Holland/Flevoland, The Netherlands, 1995–2004. Eur J Cancer 2007;43:901–8.

[30] Bergmans R, Soliman AS, Ruterbusch J, Meza R, Hirko K, Graff J, et al. Cancer incidence among Arab Americans in California, Detroit, and New Jersey SEER registries. Am J Public Health 2014;104(June (6)):e83–91.

[31] Andreoiu M, Cheng L. Multifocal prostate cancer: biologic, prognostic, and therapeutic implications. Hum Pathol 2010;41:781–93.

[32] Le JD, Tan N, Shkolyar E, Lu DY, Kwan L, Marks LS, et al. Multifocality and prostate cancer detection by multiparametric magnetic resonance imaging: correlation with whole-mount histopathology. Eur Urol 2015;67:569–76.