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Prostate Cancer Diagnosis and Management Across Twenty Years of Clinical Practice: A Single-center Experience on 2,500 Cases

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Abstract. *Background/Aim: To evaluate the diagnosis and management of prostate cancer (PCa) across twenty years of clinical practice. Materials and Methods: From January 2000 to January 2019, 7,000 patients underwent transperineal prostate biopsy and 990 went through radical prostatectomy, respectively. The clinical and pathological stage in the presence of prostate cancer (PCa) are reported here. Results: The overall number of biopsies increased over time from 1,500 (years 2000-2005) to 2,150 (years 2015-2019). PCa was found in 2,500/7,000 (37.7%) patients while the diagnosis of very low risk PCa increased from 3.2% to 13.6% and diagnosis of metastatic PCa decreased from 12% to 4%. A greater number of men with locally advanced/oligometastatic PCa underwent surgery over time with increasing numbers of nodal involvement and positive surgical margins from 5.4% and 27.2% to 10.8% and 35.6%, respectively. Conclusion: Overtreatment of PCa has been reduced over time by establishing Active Surveillance protocols. Additionally, the multidisciplinar approach has improved the management of locally advanced/oligometastatic PCa.*

Prostate cancer (PCa) is the most common type of cancer with more than 360,000 deaths per year (1), however the estimated risk of overdiagnosis from the screening protocols is equal to 50% (2). These facts highlight the necessity to separate the cases of clinically-significant prostate cancer (csPCa) from those of indolent tumors (3). During the last decade, active surveillance (AS) has become an alternative (4, 5) to radical treatment of low/very low risk PCa, focusing on the prevention of over-treating patients as well as on the strict monitoring over time. This has helped establish potential benefits of re-classification, which can justify the deferred radical treatment. In this respect, multiparametric magnetic resonance imaging (mpMRI) has been recommended for the diagnosis of csPCa in men who are candidates for prostate biopsy (6) and/or are enrolled in AS protocols (5). Finally, through a multidisciplinary approach, the introduction of robotic radical prostatectomy (RALP) in the clinical practice, advanced radiotherapy strategies, focal therapy combined with new oncological drugs, have improved the outcome of PCa patients in each clinical stage.

Here, we report the progress in the diagnosis and management of men with PCa accross twenty-years of clinical practice focusing on the clinical presentation and therapeutic strategies.

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Key Words: Prostate cancer, MRI and prostate cancer, MRI/TRUS targeted prostate biopsy, transperineal prostate biopsy, radical retropubic prostatectomy.

Patients and Methods

Patients. From January 2000 to January 2019, 7,000 men aged between 38 and 91 years (median age=61.8 years) underwent prostate biopsy under the suspicion of PCa. The indications for biopsy were: i) abnormal digital rectal examination, ii) PSA >10 ng/ml or iii) PSA values between 4.1-10 ng/ml, and 2.6-4 ng/ml with Free/Total PSA≤25% and ≤20%, respectively.

Methods. Prostate biopsy was performed transperineally using a freehand technique, a tru-cut 18-gauge needle (Bard; Covington, GA) and a GE Logiq 500 PRO ecograph (General Electric; Milwaukee, WI) supplied with a biplanar transrectal probe (5-6.5 MHz). In the case of an initial or a repeat procedure an extended (18 cores) *vs*. a saturation biopsy (SPBx: 24 cores) was done under local anaesthesia or sedation accompanied by antibiotic prophylaxis (one tablet daily of levofloxacin 500 mg for 3 days) (7). Since 2011, 1,350 candidate patients for repeat biopsy were submitted to mpMRI. In the presence of a PI-RADS (Prostate Imaging-Reporting and Data System–version 2) score≥3, a transperineal mpMRI/TRUS fusion biopsy (TPBx: 4 cores for each suspicious area) was added to SPBx (6). All mpMRI examinations were performed using a 3.0 Tesla scanner, (ACHIEVA 3T; Philips Healthcare Best, the Netherlands) equipped with: i) a 16-channel phased-array coil placed around the pelvic area with the patient in the supine position, ii) a multi-planar turbo spin-echo T2-weighted, iii) an axial

diffusion weighted imaging and iv) an axial dynamic contrast enhanced MRI (8). The TPBx was performed transperineally using a tru-cut 18-gauge needle (Bard; Covington, GA, USA) using a Hitachi 70 Arietta ecograph, (Chiba, Japan) supplied with a bi-planar transrectal probe (6). All the data were collected using the START criteria (9).

All the patients with csPCa and a life expectancy greater than ten years were candidates for definitive treatment (radical prostatectomy or external beam radiation). Since 2013, men with very low risk PCa were enrolled in an Active Surveillance protocol (10).

The diagnosis and management of PCa was evaluated across twenty-years (subdivided in four periods of 5 years (i) 2000-2004, ii) 2005-2009, iii) 2010-2014 and iv) 2015-2019 of clinical practice at a single Center, following the new diagnostic (*i.e.*, mpMRI) and therapeutic (*i.e.*, AS) strategies. In detail, biopsies and definitive specimens of men submitted to prostate biopsy and radical retropubic prostatectomy (RRP) showed changes in clinical and pathological stages over time. The Clavien-Dindo grading system for the classification of biopsy and surgery complications was used (11).

Statistics. For our statistical analysis we used the *t* Student's - test with a p-value<0.05 as statistically significant.

Results

The number of prostate biopsies and the detection rate for PCa increased over time (Table I) from 1,500 (years 2000-2005) to 2,150 (years 2015-2019) (p=0.01). On the contrary, the incidence of complications following transperineal prostate biopsy was limited during the twenty-year assessment period with respect to the number of needle cores, the number of patients with sepsis and those who needed hospital admission. In addition, only 46/7000 (0.6%) and 28/7000 (0.4%) were assigned a grade II and I of the Clavien-Dindo complications scale, respectively. The number of patients who were admitted to the emergency department was limited to 9.3% (140/1500 patients) during the period 2000-2004) and 9.5 % (905/2150) during the period 2015-2019.

The overall detection rate of PCa significantly increased from 30.6% (years 2000-2004) to 38.6% (years 2015-2019) (p=0.03); in detail, the diagnosis of low-*versus* intermediate-*versus* high-risk *versus* metastatic PCa (12) is reported in Table I. The incidence of clinical T1c PCa increased from 62 (years 2000-2004) to 69% (years 2015-2019) (p=0.03). Conversely, the diagnosis of metastatic PCa significantly decreased from 12% to 4% (p=0.01). The detection rate of very low-risk PCa significantly increased from 3.2% (26/285 cases) to 13.6% (79/572 cases) (p=0.01); therefore, since 2013, about 30 men/year were enrolled in an AS (11) protocol with a risk of upgrading/upstaging at confirmatory biopsy equal to 28%.

Among the 1,480 men candidate to definitive treatment, 490 (31%) underwent external beam radiation and 990 (69%) were submitted to RRP (Table II). The median age of men who underwent surgery progressively increased from 65.2 (range=42-71 years, period 2000-2004) to 68.3 years (range=41-79 years; period 2015-2019). The incidence of indolent PCa decreased from 3.6% (years 2000-2004) to 1% (years 2015-2019). On the contrary, a greater number of locally advanced and oligometastatic PCa, affecting manly younger men, was submitted to surgery. In fact, pT3b stage (13), nodal involvement and positive surgical margins significantly increased from 13.2%, 5.4% and 27.2% (years 2000-2004) to 18.4% (p=0.06), 10.8% (p=0.04) and 35.6% (p=0.01) (years 2015-2019), respectively (Table II). The number of nerve sparing procedures was limited during the period we evaluated because a greater number of men with very low risk PCa were included in AS protocols. The median time of surgery decreased from 150 (range=120-210 minutes) to 120 minutes (90-150 minutes) and was correlated with the surgical template used to remove the nodes. At the same time, the number of the removed nodes increased from 8 (range=2-10 nodes in the years 2000-2004) to 18 (range=9-34 nodes in the years 2015-2019) according to the PCa clinical stage.

The incidence of complications 90 days post operation following RRP was also limited over time (Table III) while, the median blood loss decreased from 420 ml (range=50-1900 ml, years 2000-2004) to 350 ml (range=50-1100 ml, years 2015-2019).

Discussion

During the last decade the diagnosis and treatment of PCa has drammatically changed enacting on reducing the risk of overdiagnosis and overtreatment (14). Active Surveillance protocols (15) have significantly reduced the risk of overtreatment in men with low-risk PCa, prooving relatively safe, during long term follow-up offering a good prognosis including men with progressive disease (upgrading or upstaging). In addition, the clinical approach for treating locally advanced and/or oligometastatic PCa (16-18) in younger men has changed due to the multidisciplinar approach methods that seems to improve life aspettancy (19). In fact, a more accurate clinical stadiation using diagnostic imaging (*i.e.*, Gallium-68 prostate-specific membrane antigen PET/TC or whole body MRI) (20) allows for a better selection of candidate patients for a sequential multidisciplinary approach instead of submitting them to aggressive surgery involving extended limphadenectomy as a first step of treatment (21, 22). At the same time, new radiotherapy strategies (23) implemented as initial, adjuvant or salvage teatments seems to improve the overall survival of the patients reducing the morbidity associated with radiotherapy. In addition, hormonal treatment (24) combined with chemotherapy (25) has demonstrated a favorable impact on the presence of metastatic PCa at diagnosis and of clinical progression. In conclusion, the therapeutic advances in the clinical management of PCa in all the clinical stages allow

Table I. *Detection rate for prostate cancer (PCa) in 7,000 men submitted to transperineal prostate biopsy during a twenty-year period (subdivided in 4 periods).*

Clinical Stage	Years 2000-04	Years 2005-09	Years 2010-14	Years 2015-19	*p*-Value
Overall prostate biopsy:					
7,000 patients (pts)	1,500	1,500	1,850	2,150	0.01
Initial Biopsy	1,050 (70%)	990 (64%)	1127 (61%)	1200 (56.8%)	0.01
Repeat Biopsy	450 (30%)	510 (34%)	723 (39%)	950 (44.2%)	0.01
Overall PCa: 2,500 (35.7%)	460 (30.6%)	510 (34%)	700 (37.8%)	830 (38.6%)	0.03
Low risk PCa	62% (285 pts)	62.3% (318 pts)	62.1% (435 pts)	69% (572 pts)	0.03
Intermediate risk PCa	18.5% (85 pts)	18.7% (95 pts)	19.2% (135 pts)	18.4% (153 pts)	0.33
High risk PCa	7.5% (35 pts)	8% (41 pts)	9.2% (64 pts)	8.6% (72 pts)	0.35
Metastatic PCa	12.0% (55 pts)	11% (56 pts)	9.5% (66 pts)	4.0% (33 pts)	0.01

Table II. *Pathological staging of 990 men submitted to radical retropubic prostatectomy (RRP) during a twenty-year period (subdivided in 4 periods).*

Pathological Stage (pTN)	Years 2000-04	Years 2005-09	Years 2010-14	Years 2015-19	*p*-Value
Number of RRP	220	260	307	203	
Overall: 990 patients (pts)	22.3%	26.2%	31%	20.5%	0.32
Indolent PCa (Gleason score 6 and cancer volume <0.5 ml)	3.6% (8 pts)	3.8% (10 pts)	1.6% (5 pts)	0.9% (2 pts)	0.02
pT2c					
Overall: 463 pts	48.2% (106 pts)	48.5% (126 pts)	50.5% (155 pts)	45.8% (93 pts)	0.15
pT3a					
Overall: 315 pts	35.0% (77 pts)	33.1% (86 pts)	34.2% (105 pts)	34.5% (70 pts)	0.32
pT3b					
Overall: 139 pts	13.2% (29 pts)	14.6% (38 pts)	13.7% (42 pts)	18.8% (38 pts)	0.06
Positive nodes	5.4% (12 pts)	5.8% (15 pts)	6.8% (21 pts)	11.3% (23 pts)	0.04
Positive surgical margins	27.2% (60 pts)	26.5% (69 pts)	30.6% (94 pts)	35.9% (73 pz)	0.01

Table III. *Post-operative complications following radical retropubic prostatectomy (RRP) during a twenty-year period (subdivided in 4 periods).*

90-day post-Operative Complications post RRP	Years 2000-04	Years 2005-10	Years 2011-14	Years 2015-19	*p*-Value
Clavien-Dindo I	5%	5.7%	5.2%	4.9%	0.34
Clavien-Dindo II	2.7%	2.7%	2.9%	2.9%	0.38
Clavien-Dindo IIIa	1.8%	1.9%	2.2%	1.9%	0.33
Clavien-Dindo IIIb	0.9%	1.1%	0.9%	0.9%	0.42
Trasfusion rate	7.2%	7.7%	6.2%	5.9%	0.35
Rectal injury	1.3%	1.1%	1.3%	1%	0.42
Symptomatic pelvic lymphocele	8.2%	8.8%	9.1%	9.8%	0.34
Anastomotic stenosis	11.3%	10.4%	9.1%	8.8%	0.34

for a tailored treatment using a multidisciplinary approach, in the context of a dedicated Prostate Cancer Unit (26).

In our series, which refer to 7,000 prostate biopsies and 990 RRP, during twenty-years of clinical practice we have reported the safety of the transperineal prostate biopsy with an estimated risk of sepsis equal to zero. This result should be taken into consideration in clinical practice due to the increased antibiotic resistance and the considerable risk of sepsis in men submitted to transrectal biopsy (27, 28). The overall number of prostate biopsies significantly increased

over time from 1,500 (years 2000-2004) to 2,150 (years 2015-2019), the diagnosis of very low risk PCa significantly increased from 3.2% (26/285 cases) to 13.6% (79/572 cases) and, at the same time, metastatic PCa significantly decreased from 12% to 4%, in accordance with the results of the screening protocols. At the same time, the number of RRP decreased progressively, while a greater number of yourger men with locally advanced/oligometastatic PCa were submitted to surgery over time. In detail, pT3b stages, nodes involvement and positive surgical margins increased from 13.2%, 5.4% and 27.2% (years 2000-2004) to 18.4%, 10.8% and 35.6% (years 2015-2019), respectively. In addition, the number of nodes removed increased from 8 (rage: 2-10 nodes, years 2000-2004) to 18 (range: 9-34 nodes, years 2015-2019) depending on the clinical stage of the patient.

Regarding our results some considerations should be made. Firstly, the study is retrospective. Secondly, the surgical approach refers only to open RRP because in our Hospital we do not possess a robotic platform. Interestingly, this means that the study reflects the real clinical pratice of many geographic areas where minimally invasive surgery (RALP) cannot yet be performed (29, 30). Finally, the execution of RRP could have been selected for a greater number of locally advanced/oligometastatic PCa patients, while low- and intermediate-risk PCa patients suitable for nerve-sparing surgery were referred for a RALP approach.

The management of PCa needs a tailored approach to improve the patient's quality of life. In our twenty years of experience, the risk of over-treatment has been reduced by establishing AS protocols, while at the same time, the multidisciplinary approach has significantly improved the management of locally advanced/oligometastatic PCa.

Conflicts of Interest

The Authors declare no conflict of Interest exists in regard to this study.

Authors' Contributions

The Authors contributed equally to this article.

References

1 Pishgar F, Ebrahimi H, Saeedi Moghaddam S, Fitzmaurice C and Amini E: Global, Regional and National Burden of Prostate Cancer, 1990 to 2015: Results from the Global Burden of Disease Study 2015. J Urol *199*: 1224-1232, 2018. PMID: 29129779, DOI: 10.1016/j.juro.2017.10.044.

2 Schröder FH, Hugosson J, Roobol MJ, Tammela TL, Zappa M, Nelen V, Kwiatkowski M, Lujan M, Määttänen L, Lilja H, Denis LJ, Recker F, Paez A, Bangma CH, Carlsson S, Puliti D, Villers A, Rebillard X, Hakama M, Stenman UH, Kujala P, Taari K, Aus G, Huber A, van der Kwast TH, van Schaik RH, de Koning HJ, Moss SM, Auvinen A and ERSPC Investigators: Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. Lancet *384*: 2027-2035, 2014. PMID: 25108889, DOI: 10.1016/S0140-6736(14)60525-0.

3 Valerio M, Anele C, Bott SR, Charman SC, van der Meulen J, El-Mahallawi H, Emara AM, Freeman A, Jameson C, Hindley RG, Montgomery BSI, Singh PB, Ahmed HU and Emberton M: The prevalence of clinically significant prostate cancer according to commonly used histological thresholds in men undergoing template prostate mapping bopsies. J Urol *195*: 1403-1408, 2016. PMID: 26626221, DOI: 10.1016/j.juro.2015.11.047.

4 Filson CP, Natarajan S, Margolis DJ, Huang J, Lieu P, Dorey FJ, Reiter RE and Marks LS: Prostate cancer detection with magnetic resonance-ultrasound fusion biopsy: The role of systematic and targeted biopsies. Cancer *122*: 884-892, 2016. PMID: 2674914, DOI: 10.1002/cncr.29874.

5 Pepe P, Garufi A, Priolo G and Pennisi M: Can MRI/TRUS fusion targeted biopsy replace saturation prostate biopsy in the re-evaluation of men in active surveillance? World J Urol *34*: 1249-1453, 2016. PMID: 26699628, DOI: 10.1007/s00345-015-1749-3.

6 Pepe P, Garufi A, Priolo GD, Galia A, Fraggetta F and Pennisi M: Is it time to perform only MRI targeted biopsy? Our experience in 1032 men submitted to prostate biopsy. J Urol *200*: 774-778, 2018. PMID: 29679618, DOI: 10.1016/j.juro. 2018.04.061.

7 Pepe P and Aragona F: Saturation prostate needle biopsy and prostate cancer detection at initial and repeat evaluation. Urology *70*: 1131-1135, 2007. PMID: 18158033.

8 Pepe P, Garufi A, Priolo G, Candiano G, Pietropaolo F, Pennisi M, Fraggetta F and Aragona F: Prostate cancer detection at repeat biopsy biopsy: Can pelvic phased-array multiparametric MRI replace saturation biopsy? Anticancer Res *33*: 1195-1199, 2013. PMID: 23482802.

9 Moore CM, Kasivisvanathan V, Scott Eggener S, Emberton M, Fütterer JJ, Gill IS, Grubb Iii RL, Hadaschik B, Klotz L, Margolis DJ, Marks LS, Melamed J, Oto A, Palmer SL, Pinto P, Puech P, Punwani S, Rosenkrantz AB, Schoots IG, Simon R, Taneja SS, Turkbey B, Ukimura O, van der Meulen J, Villers A, Watanabe Y and START Consortium: Standards of Reporting for MRI-targeted Biopsy Studies (START) of the Prostate: Recommendations from an International Working Group. Eur Urol *64*: 544-552, 2013. PMID: 23537686, DOI: 10.1016/j.eururo.2013.03.030.

10 Pepe P, Cimino S, Garufi A, Priolo G, Russo GI, Giardina R, Reale G, Pennisi M and Morgia G: Confirmatory biopsy of men under active surveillance: extended *versus* saturation *versus* multiparametric magnetic resonance imaging/transrectal ultrasound fusion prostate biopsy. Scand J Urol *51*: 260-263, 2017. PMID: 28513296, DOI: 10.1080/21681805.2017.1313310.

11 Dindo D, Demartines N and Clavien PA: Classification of surgical complications. A new proposal with evaluation in a Cohort of 6336 patients and results of survey. Ann Surg *2*: 205-213, 2004. PMID: 15273542.

12 D'Amico AV, Renshaw AA, Cote K, Hurwitz M, Beard C, Loffredo M and Chen MH: Impact of the percentage of positive prostate cores on prostate cancer-specific mortality for patients with low or favourable intermediate-risk disease. J Clin Oncol *22*: 3726-3732, 2004. PMID: 15365069, DOI: 10.1200/JCO.2004.01.164.

13 Pepe P, Improta G, Fraggetta F, Emmanuele C, Simeon V, Dibenedetto G, Colecchia M and Aragona F: PSA nadir and outcome in 100 patients with pT3b prostate cancer. Anticancer Res *34*: 937-941, 2014. PMID: 24511036.

14 Trama A, Botta L, Nicolai N, Rossi PG, Contiero P, Fusco M, Lodde M, Pannozzo F, Piffer S, Puppo A, Seeber A, Tumino R, Valdagni R, Gatta G and Prostate Cancer High Resolution Study Working Group: Prostate cancer changes in clinical presentation and treatments in two decades: an Italian population-based study. Eur J Cancer *67*: 91-98, 2016. PMID: 27620947, DOI: 10.1016/j.ejca.2016.07.021.

15 Bokhorst LP, Valdagni R, Rannikko A, Kakehi Y, Pickles T, Bangma CH, Roobol MJ and PRIAS study group: A decade of active surveillance in the PRIAS study. An update and evaluation of the criteria used to recommend a switch to active treatment. Eur Urol pii: S0302-2838(16)30277-9, 2016. PMID: 27329565, DOI: 10.1016/j.eururo.2016.06.007.

16 Delporte G, Henon F, Ploussard G, Briganti A, Rizk J, Rozet F, Touijer K and Ouzzane A: Radical prostatectomy for locally advanced and high-risk prostate cancer: A systematic review of the literature. Prog Urol *28*: 875-889, 2018. PMID: 30262263, DOI: 10.1016/j.purol.2018.08.007. Epub 2018 Sep 24.

17 Beck V, Schlenker B, Herlemann A, Apfelbeck M, Buchner A, Gratzke C, Stief CG and Tritschler S: The increase of stage, grading, and metastases in patients undergoing radical prostatectomyduring the last decade. World J Urol, 2018. PMID: 30225798, DOI: 10.1007/s00345-018-2487-0.

18 Bandini M, Marchioni M, Preisser F, Zaffuto E, Tian Z, Tilki D, Montorsi F, Shariat SF, Saad F, Briganti A and Karakiewicz PI: Survival after radical prostatectomy or radiotherapy for locally advanced (cT3) prostate cancer. World J Urol *36*: 1399-1407, 2018. PMID: 29717358, DOI: 10.1007/s00345-018-2310-y.

19 Preisser F, Mazzone E, Nazzani S, Bandini M, Tian Z, Marchioni M, Steuber T, Saad F, Montorsi F, Shariat SF, Huland H, Graefen M, Tilki D and Karakiewicz PI: Comparison of perioperative outcomes between cytoreductive radical prostatectomy and radical prostatectomy for nonmetastatic prostate cancer. Eur Urol *74*: 693-696, 2018. PMID: 30037529, DOI: 10.1016/j.eururo.2018.07.006.

20 Lecouvet FE, Oprea-Lager DE, Liu Y, Ost P, Bidaut L, Collette L, Deroose CM, Goffin K, Herrmann K, Hoekstra OS, Kramer G, Lievens Y, Lopci E, Pasquier D, Petersen LJ, Talbot JN, Zacho H, Tombal B and deSouza NM: Use of modern imaging methods to facilitate trials of metastasis-directed therapy for oligometastatic disease in prostate cancer: a consensus recommendation from the EORTC Imaging Group. Lancet Oncol *19(10)*: e534-e545, 2018. PMID: 30303127, DOI: 10.1016/S1470-2045(18)30571-0.

21 Gandaglia G, Soligo M, Battaglia A, Muilwijk T, Robesti D, Mazzone E, Barletta F, Fossati N, Moschini M, Bandini M, Joniau S, Karnes RJ, Montorsi F and Briganti A: Which patients with clinically node-positive prostate cancer should be considered for radical prostatectomy as part of multimodal treatment? The impact of nodal burden on long-term outcomes. Eur Urol pii: S0302-2838(18)30837-6, 2018. PMID: 30409676, DOI: 10.1016/j.eururo.2018.10.042.

22 Huang H, Muscatelli S, Naslund M, Badiyan SN, Kaiser A and Siddiqui MM: Evaluation of cancer specific mortality with surgery *versus* radiation as primary therapy for localized high grade prostate cancer in men younger than 60 years. J Urol *201*: 120-128, 2019. PMID: 30577404, DOI: 10.1016/j.juro.2018.07.049.

23 Spence W: Personalising prostate radiotherapy in the era of precision medicine: A review. J Med Imaging Radiat Sci *49*: 376-382, 2018. PMID: 30514554, DOI: 10.1016/j.jmir.2018.01.002.

24 Khalaf DJ, Sunderland K, Eigl BJ, Kollmannsberger CK, Ivanov N, Finch DL, Oja C, Vergidis J, Zulfiqar M, Gleave ME and Chi KN: Health-related Quality of life for abiraterone plus prednisone *versus* enzalutamide in patients with metastatic castration-resistant prostate cancer: Results from a phase II randomized trial. Eur Urol pii: S0302-2838(18)31020-0, 2018. PMID: 30591354, DOI: 10.1016/j.eururo.2018.12.015.

25 Halabi S, Dutta S, Tangen CM, Rosenthal M, Petrylak DP, Thompson IM Jr, Chi KN, Araujo JC, Logothetis C, Quinn DI, Fizazi K, Morris MJ, Eisenberger MA, George DJ, De Bono JS, Higano CS, Tannock IF, Small EJ and Kelly WK: Overall survival of black and white men with metastatic castration-resistant prostate cancer treated with docetaxel. J Clin Oncol JCO1801279, 2018. PMID: 30576268, DOI: 10.1200/JCO.18.01279.

26 Kinnear N, Smith R, Hennessey DB, Bolton D and Sengupta S: Implementation rates of uro-oncology multidisciplinary meeting decisions. BJU Int *120(Suppl 3)*: 15-20, 2017. PMID: 28719043, DOI: 10.1111/bju.13892.

27 Pepe P and Aragona F: Morbidity following transperineal prostate biopsy in 3,000 patients submitted to 12 *vs*. 18 *vs*. more than 24 needle cores. Urology *81*: 1142-1146, 2013. PMID: 23726443, DOI: 10.1016/j.urology.2013.02.019.

28 Grummet J: How to Biopsy: Transperineal *versus* transrectal, saturation *versus* targeted, what's the evidence? Urol Clin North Am *44*: 525-534, 2017. PMID: 29107269, DOI: 10.1016/j.ucl.2017.07.002.

29 Ilic D, Evans SM, Allan CA, Jung JH, Murphy D and Frydenberg M: Laparoscopic and robot-assisted *vs*. open radical prostatectomy for the treatment of localized prostate cancer: a Cochrane systematic review. BJU Int *121*: 845-853, 2018. PMID: 29063728, DOI: 10.1111/bju.14062.

30 Preisser F , Nazzani S , Mazzone E, Knipper S, Bandini M, Tian Z, Haese A, Saad F, Zorn KC, Montorsi F, Shariat SF, Graefen M, Tilki D and Karakiewicz PI: Regional differences in total hospital charges between open and robotically assisted radical prostatectomy in the United States. World J Urol, 2018. PMID: 30315358, DOI: 10.1007/s00345-018-2525-y.

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