Asian Journal of Urology (2019) 6, 123–124

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajur

Editorial

Prostate cancer: On the road of progress

In Europe, prostate cancer (PCa) is the most frequently diagnosed cancer in men with an estimated 416 000 new cases and the third leading cause of cancer death with 92 000 deaths in 2012 [1]. In China, based on 177 of 234 cancer registries, PCa was the 7th most frequent neoplasm in men, with 49 000 new cases in 2011 [2]. Of course the variability of the incidence of PCa has many causes, including environmental, dietary, lifestyle factors or genetic risks, with the well-known example of the higher incidence in African-American men compared to that of Caucasian men in the United States. In addition, the incidence rate is also greatly influenced by the more and more frequent testing of prostate-specific antigen (PSA) in asymptomatic men, as seen in Europe and United States since the 1980s [3]. Today, early diagnosis is possible in men aged 50–75 years, but since PCa encompasses a wide variety of situations, from asymptomatic, low risks cancers to highly aggressive, life-threatening diseases, it is critical that physicians take into account age, co-morbidity, baseline PSA, prostate volume and velocity, to inform their patients about the risks and benefits of a prostate biopsy and of all available therapeutic options. The treatment, depending on an overall assessment of TNM and D'Amico classification, should be discussed with the patient after a multidisciplinary conference or tumor board, and according to national or European Association of Urology Guidelines. At one end of the spectrum, some patients do not need any treatment at all, some others are candidates for an active surveillance with deferred treatment, and at the other end of the spectrum some patients need to be treated without delay. In this regard, the present special issue of *Asian Journal of Urology* is an update of many aspects of PCa in the late 2010s, including current diagnosis, imaging, active surveillance, surgery, radiotherapy and systemic treatments. Worldwide renowned specialists involved in clinical research have participated to this issue aiming at sharing their experience. More information about epidemiology, chemoprevention, screening, anatomo-pathology, biomarkers, genomics and nuclear medicine can be found in the 2017 edition of the European Association of Urology Guidelines [4] and the book entitled *Management of Prostate Cancer, A Multidisciplinary Approach* [5].

Descotes [6] in his comprehensive overview of the diagnosis of PCa, reminds us that following PSA blood tests, transrectal ultrasound (TRUS)-guided prostate biopsy remains the gold standard to confirm the diagnosis. However, the false negative or undergrading rate of TRUS is high, requiring more sophisticated methods. A series of new and refined tests were created to improve the accuracy of PSA. PSA is not specific of PCa, with no universally accepted threshold values. Thus methods to optimize this test were developed and studied on a large scale, like the PSA aged adjusted, the ratio of free PSA/PSA, PSA density, PSA velocity and PSA doubling time, all of which presenting some advantages and limitations, as clearly discussed by the author. Other blood or urine tests like the prostate health index (Phi), the four kallikrein panel score (4 K score), the *prostate cancer gene 3* (*PCA 3*) score seem to be promising and can be used as additional tools. Descotes also provides interesting data on how to improve TRUS techniques such as the perineal approach, the magnetic resonance imaging (MRI)-TRUS fusion biopsy, or the multiparametric MRI (mpMRI) guided biopsy. The remaining of the review focuses on local staging, lymph node staging and the search of distant bone metastases.

Rouvière and Moldovan [7] discuss extensively the role of prostate mpMRI: mpMRI combines T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE). The authors comment on the diagnostic criteria for PCa including the subjective Lickert score and the semi-objective lesion features of the Prostate Imaging Reporting and Data System (PI-RADS) scoring system. These scores predict not only the likelihood of malignancy but also the aggressiveness of the tumor. For the evaluation of extra-capsular extension (ECE) or seminal vesicle invasion (SVI), mpMRI specificity seems to be good but sensitivity is low in case of microscopic ECE or SVI. The sensitivity of mpMRI is excellent for PCa with a Gleason score $\geq$7 with a volume of $\geq$0.5 mL. The negative predictive value (NPV) of mpMRI appears excellent, but it should be interpreted in the light of the patient's classical risks for PCa, and nomograms combining mpMRI and known predictors like age, PSA density, digital rectal examination (DRE), *etc.* should be used in the future to decide whether a biopsy should be done or not.

https://doi.org/10.1016/j.ajur.2019.01.002

Klotz [8] speaks in favor of active surveillance to manage the risk of overtreatment due to mass or individual screening. Eligible patients are those with grade group 1 (Gleason score 6) or selected patients with grade group 2 (Gleason score 3 + 4) with a low percentage of pattern 4. Patients are followed up with serial PSA assessments and repeat biopsies, and initial confirmatory biopsy should be performed within the first 6–12 months; the actuarial 15-year PCa mortality rate is 5%. With a restrictive approach, the Hopkins group [9] advises surveillance to patients who meet the following criteria: Gleason 6 with no more than 2 positive cores, no core >50% involved, and PSA density <0.15. If these criteria are met, the 15-year PCa mortality rate is as low as 0.5%.

Van Poppel et al. [10] remind us that retropubic radical prostatectomy is not the "gold standard" any more for locally confined PCa, since minimally invasive techniques as laparoscopy have appeared, and recently robotic surgical technologies have revolutionized PCa surgery. No data prove the superiority of any surgical approach in terms of oncological outcomes. Over the years the complication rates of radical prostatectomy have become very limited with improved cancer control and better functional results. The indications and the surgical technique of radical open and laparoscopic prostatectomy, eventually robot-assisted as well as the pre- and post-operative measures and the surgery-related consequences, are reviewed.

Bolla et al. [11] mention that intensity modulated radiotherapy (IMRT) is the gold standard for external beam radiotherapy. Patients with low-risk localized PCa can be treated by IMRT or brachytherapy. Intermediate-risk patients may benefit from IMRT combined with 4–6 months of androgen deprivation therapy (ADT); should the patients be reluctant to ADT, they can be offered IMRT alone or combined with brachytherapy. High-risk patients require IMRT with long-term (≥2 years) ADT. Post-operative irradiation, either immediate or early deferred, is proposed to patients classified as pT3 pN0 with undetectable PSA, based on surgical margins, Gleason score and quality of life; early salvage is another option provided that irradiation starts with PSA value ≤0.5 ng/mL.

Gravis [12] relates the whole story of the management of metastatic PCa with randomized phase III trials from 2004 onwards. The addition of docetaxel to ADT versus ADT alone in the castration sensitive metastatic setting has resulted in a significant overall survival benefit particularly for high volume disease. The landscape of metastatic castration resistant PCa is moving and the choice of first line treatment has to be based on performance status, symptoms, comorbidities location and extent of disease. The future belongs to the identification of new subtypes with molecular characterization and new therapeutic targets.

In conclusion, active surveillance has become a therapeutic option as shown by the results of the Toronto and Hopkins groups and the Protect trial [13]; the grading model established by the International Society of Urological Pathology [14] makes easier the therapeutic de-escalation with Gleason score 6 classified as Grade 1, the latter having an insignificant risk of metastasis. Tumor boards help urologists and radiation oncologists to offer a personalized treatment to the patients, based on levels of evidence, which can be modulated according to their characteristics and desires, but specialists must be aware that their techniques have to satisfy quality assurance criteria. Therapeutic algorithms of chemical castration resistant PCa, with chemotherapy and new hormonal manipulations have improved overall survival and quality of life of patients, and the challenge for medical oncologists is now to find the optimal sequencing.

References

[1] Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe : estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374–403.

[2] Chen W, Zheng R, Zeng H, Zhang S. The updated incidences and mortalities of major cancer in China, 2011. Chin J Cancer 2015;34:502–7.

[3] Hankey BF, Feuer EJ, Clegg LX, Hayes RB, Legler JM, Prorok PC, et al. Cancer surveillance series : interpreting trends in prostate cancer-part I : evidence of the effects of screening in recent prostate incidence. J Natl Cancer Inst 1999;91:1017–24.

[4] Mottet N, Bellmunt J, Briers and members of the EAU-ESTRO-ESUR-SIOG. Guidelines panel on Prostate Cancer. [accessed 26 December 2018]. http://uroweb.org/guideline/prostate-cancer/.

[5] Bolla M, van Poppel H. Management of prostate cancer. A multidisciplinary approach. 2nd ed. Switzerland: Springer; 2017. p. 1–141.

[6] Descotes JL. Diagnosis of prostate cancer. Asian J Urol 2019;6:129–36.

[7] Rouvière O, Moldovan PC. The current role of prostate multiparametric magnetic resonance imaging. Asian J Urol 2019;6:137–45.

[8] Klotz L. Contemporary approach to active surveillance for favorable risk prostate cancer. Asian J Urol 2019;6:146–52.

[9] Tosoian JJ, Trock BJ, Landis P, Feng Z, Epstein JI, Partin AW, et al. Active surveillance program for prostatic cancer : an update of the John Hopkins experience. J Clin Oncol 2011;29:2185–90.

[10] Van Poppel H, Everaerts W, Tosco L, Joniau S. Open and robotic radical prostatectomy. Asian J Urol 2019;6:125–8.

[11] Bolla M, Henry A, Mason M, Wiegel T. The role of radiotherapy in locally advanced prostate cancer. Asian J Urol 2019;6:153–61.

[12] Gravis G. Systemic treatment for metastatic prostate cancer. Asian J Urol 2019;6:162–8.

[13] Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 2016;375:1415–24.

[14] Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA, et al. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma : definition of grading patterns and proposal of a new grading system. Am J Surg Pathol 2016;40:244–52.

Michel Bolla
Radiation Oncology, Grenoble Alpes University, Grenoble, France
E-mail address: mbolla@chu-grenoble.fr

René-Olivier Mirimanoff
Radiation Oncology, University Hospital (CHUV), Lausanne, Switzerland
E-mail address: rene-olivier.mirimanoff@chuv.ch