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INVITED EDITORIAL

Prostate Cancer

The continued pursuit of new strategies and new technologies

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The incidence of prostate cancer (PCa) is increased in the last years to become the second leading cause of death in males.[1] In this context, low-risk and intermediate-risk PCa are the most represented clinical patterns and undoubtedly most subjected to technological innovations. In fact, the diagnosis and management of PCa have dramatically evolved in the last two decades with the advent of robotics, proton-beam radiation as well as magnetic resonance imaging (MRI) and prostate-specific membrane antigen-positron emission tomography (PSMA-PET).[2] At the same time, we know from nomograms that biological aggressiveness correlates with lymph node invasion and recently with testosteronemia.[3]

The aim of this special issue has been to analyze the most recent diagnostic and therapeutic options available in the area of low- and intermediate-risk PCa thanks to the expertise of researchers working in this pathological field. However, before going into the heart of the topic, it seems necessary to point out the role of the screening because it allows the epidemiological characterization of PCa.[4] In this sense, screening programs allowed us over the years to diagnose PCa in the early stages and to define its different aggressiveness. In this setting, the screening has also indirectly contributed to the development of important diagnostic and therapeutic innovations aimed at achieving an optimal compromise between tumor prevention and tumor curability to maintain an acceptable quality of life. In particular, the use of new and existing biomarkers such as prostate cancer antigen 3 (PCA3), transmembrane protease serine 2 (TMPRSS2), and others at the serum, urinary, and tissue levels could be used to implement prostate-specific antigen (PSA) to detect particular forms of cancer and improve its overall diagnostic accuracy.[5,6] In this way, the endogenous testosterone assay also plays an innovative diagnostic and predictive role in the relationship with low- and intermediate-risk PCa. In fact, the association between endogenous testosterone and the European Association of Urology (EAU) risk classes, and the association between endogenous testosterone and tumor upgrading or upstaging is scientifically evident. In this respect, it was revisited the pathophysiology of endocrine tumor dependence introducing new concepts related to testosterone variations in association with the aggressiveness of the neoplasm and focusing on the role of testosterone in the current diagnostic workflow.[7] In this new interpretation of the pathophysiology of low- and intermediate-risk PCa, histopathological grading is also of high interest with particular reference to the identification of pattern 4 which includes ill-formed or fused glands. In fact, there is an evident inconsistency among pathologists in recognizing these glands, especially when mixed with pattern 3. In this regard, it was carefully reviewed this issue and pointed out that the cribriform pattern is associated with the most severe prognosis among the subtypes of pattern 4. This tool represents an essential characterization for the optimization of therapeutic treatment in the case of active surveillance (AS).[8] At present, an accurate pathological diagnosis of low- and intermediate-risk PCa is crucial to indicate conservative treatment such as AS, as several studies have shown that patients with early and moderately differentiated PCa can avoid active treatment as they have a low mortality rate.[9] Undoubtedly in patients undergoing AS, the role of PSA is essential for the follow-up of the disease, as they are imaging investigations such as MRI and PSMA-PET/computed tomography (CT). In particular, although the latter shows limited efficacy in routine staging due to minimal uptake in low-grade tumors, it seems to be effective in differentiating between low- and high-grade tumors, and thus with potential application in patients who are candidates for AS.[10] It is, therefore, clear that a clinical predictivity is also an essential tool in the decision-making process. In this regard, Briganti's 2012 nomogram was found to be an independent predictor of PCa progression in the intermediate-risk class of EAU in patients undergoing robot-assisted radical prostatectomy (RARP). This finding, therefore, allows us to observe the strong association between Briganti's nomogram and the natural history of PCa by applying the concept of artificial intelligence that should accompany us in decision-making in these patients.[11] From this point of view, in relation to the new minimally invasive therapies, we cannot disregard the concept of clinical predictivity for their correct and routine application. At present, we are watching new strategies such as focal therapy, which could represent an ideal approach for localized small-volume tumors with important advantages for the preservation of urinary continence and erection.[12] In this direction, a narrative review was reported on the different treatment modalities of high-intensity focused ultrasound (HIFU) and how nonwhole-gland ablation offers short-term results similar with whole-gland ablation.[13] Obviously, the results need to be confirmed in the long term by longitudinal randomized studies in comparison with the current reference therapies to optimize new indications of treatment.

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It has been a pleasure to work with this group of esteemed colleagues because it has been possible to produce this special issue.

CONCLUSIONS

Low- and intermediate-risk prostate cancer represents an important laboratory of clinical research. Indeed, based on the intrinsic biological activity of this type of tumor, we are now witnessing a series of diagnostic and therapeutic innovations that will surely bring about a Copernican Revolution in the next decade. In conclusion, the application of new technologies will allow us to revise the current diagnostic and therapeutic standards, resulting in a reduction of traditional therapeutic procedures in favor of minimally invasive ones and consequent preservation of quality of life. All this will only be feasible in the presence of an active multidisciplinary research as that already exists in most clinical settings.

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