EDITORIAL

Non-metastatic castration-resistant prostate cancer (CPRCM0), an old scenario with renewed clinical interest

Cáncer de próstata resistente a castración no diseminado (CPRCM0), un viejo escenario con interés clínico renovado

The questionable use of androgen suppression in patients with non-metastatic prostate cancer means that often we attend the diagnosis of resistance to castration before the cancer is metastatic (CPRCM0), without having to date a valid therapeutic alternative in this scenario. Most of these patients come from different population groups. Probably the largest is for those who develop biochemical failure after radical prostatectomy and who have received adjuvant or salvage radiotherapy. Another group of patients is made up of patients who have not received radiotherapy because they had a biochemical relapse with high-risk criteria for dissemination, and, finally, the group of patients who were treated with radical purpose by means of radiotherapy and neoadjuvant hormone therapy for periods ranging between 6 months and 3 years. The whole sum of these patients currently represents over 80% of those who reach the castration-resistant status.¹

The current scenario incorporates type I evidence, which proves the effectiveness of new forms of hormone therapy in patients with CRPC and disseminated disease, asymptomatic or mildly symptomatic.² These new therapeutic modalities come to occupy a treatment niche in which the use of chemotherapy was very discussed, since docetaxel used to be indicated only in symptomatic patients and in those asymptomatic with poor prognostic criteria.³ The currently available data with the new drugs show that their greatest efficacy is found in asymptomatic or minimally symptomatic patients. Consequently, it seems logical to think that now before a patient with CPRCM0, we must attempt to perform the early diagnosis of metastatic involvement. Thus, those patients would have the opportunity to obtain the maximum benefit from these treatments. Is that so? or are we facing a new scenario where increased survival is only the result of a bias in time, produced by starting a treatment before? The answer to this question is complex and it could only be answered by a prospective and randomized study, specifically designed to answer this question.

Early identification of dissemination in patients with CPRCM0 requires a proactive attitude to detect metastases. The problem lies in the lack of sensitivity of the conventionally used imaging tests (bone scan, computed tomography, conventional MRI) to detect dissemination.⁴ The study of the control arm of the clinical trial that compared denosumab with placebo in the prevention of bone metastases in patients with high risk of dissemination (CPRCM0 and PSA greater than 8 or PSADT <10 months) has provided valuable information defining a geometric increase in the likelihood of developing bone metastases when the PSA doubling time is shorter than 6 months; however, this study does not provide information about other metastatic sites.⁵

Positron-emission tomography (PET-CT), performed with choline, has been studied mainly in patients with biochemical relapse after radical prostatectomy and its effectiveness is discreet in patients with serum PSA levels lower than 1 ng/ml.⁶ A recent meta-analysis has shown that the sensitivity of choline PET-CT in these patients is associated with the PSA kinetics.⁷ The only study reported in the literature, which analyzes the effectiveness of choline PET-CT in patients with CRPC, and therefore with serum PSA greater than 2 ng/ml shows efficacy greater than 80%, ranging from 63% when the PSA is lower than 5 ng/ml and 86% when the PSA is greater.⁸ In this series of 157 patients, a significant ratio of the positivity of the test with the PSA kinetics was also observed. Another very recent study found a significant relationship between the findings of choline PET-CT and survival of patients with CRPC after radical prostatectomy. The

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positivity of PET-CT, the serum PSA level, and a sum of Gleason greater than 7 were independent factors in predicting cancer-specific survival. Whole-body magnetic resonance imaging (WBMRI) with diffusion is another alternative for exploring the presence of metastases in these patients. To date, only one study has compared the effectiveness of PET-CT and RMCE in diagnosing bone metastases in patients with prostate cancer. This study was conducted in 49 patients with high-risk prostate cancer in the context of their initial staging, and it concludes that PET-CT would be a more sensitive test but somewhat less specific than RMCE.

We would like to conclude by suggesting first that the use of new forms of effective treatment in patients with asymptomatic CRPCM0 requires a proactive attitude in the early diagnosis of the dissemination. Secondly, that in this scenario the choline PET-CT or RMCE would be the most effective tests to evidence early dissemination. Third, that some studies must be conducted to refine more precisely the performance of these tests based on some clinical parameters, especially serum PSA level and its kinetics, and define the sequence in case of negativity. Finally, we have to point out that this scenario may be relevant in time until effective treatments are approved for CRPCM0 or because the incidence of these patients is reduced due to better use of androgen suppression.

References


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