Actas Urol Esp. 2014;38(10):685–693

Actas Urológicas Españolas

www.elsevier.es/actasuro

REVIEW ARTICLE

Bone health in patients with prostate cancer☆

B. Miñana[a,*], J.M. Cózar[b], A. Alcaraz[c], J. Morote[d], F.J. Gómez-Veiga[e], E. Solsona[f], A. Rodríguez-Antolín[g], J. Carballido[h]

[a] *Servicio de Urología, Hospital Morales Meseguer, Universidad Católica San Antonio, UCAM, Murcia, Spain*
[b] *Servicio de Urología, Hospital Virgen de las Nieves, Granada, Spain*
[c] *Servicio de Urología, Hospital Clínic, Barcelona, Spain*
[d] *Servicio de Urología, Hospital Vall de Hebrón, Barcelona, Spain*
[e] *Servicio de Urología, CHUAC, A Coruña, Spain*
[f] *Servicio de Urología, IVO, Valencia, Spain*
[g] *Servicio de Urología, Hospital Doce de Octubre, Madrid, Spain*
[h] *Servicio de Urología, Hospital Puerta de Hierro, Madrid, Spain*

Received 17 March 2014; accepted 5 May 2014
Available online 11 November 2014

KEYWORDS
Prostate cancer;
Castration;
Bone metastases;
Fracture;
Osteoporosis;
Osteopenia;
Bisphosphonates;
Monoclonal antibody

Abstract

Context: In patients with prostate cancer, bone health is compromised by advanced age at diagnosis, androgen suppression treatments and the development of bone metastases. In this paper the medical literature is reviewed in order to update the state of the art on their incidence, prevention and management.

Evidence acquisition: A literature review about bone involvement in patients with prostate cancer in different clinical settings is performed.

Synthesis of the evidence: Decreased bone mineral density is higher in patients diagnosed of prostate cancer before starting treatment than in healthy men with the same age. During the first year of treatment, a severe loss of bone density is reported due to androgen suppression therapy. From then on, loss of bone density seems to slow down, persisting at long-term. It is important to know the starting point and the dynamics of bone loss in order to prevent its progression. The skeletal events have an important impact on quality of life in patients with prostate cancer. Both denosumab and zoledronic acid have proven effective in reducing bone loss.

Conclusions: The prevention and management of bone involvement in patients with prostate cancer are critical to quality of life in these patients and require an individualized approach. Before starting a prolonged androgen deprivation, baseline risk of fracture should be evaluated in order to adopt the proper protective measures. In patients with metastases, early treatments reducing the risk of bone events should be taken into account.

☆ Please cite this article as: Miñana B, Cózar JM, Alcaraz A, Morote J, Gómez-Veiga FJ, Solsona E, et al. Salud ósea en pacientes con cáncer de próstata. Actas Urol Esp. 2014;38:685–693.

* Corresponding author.
E-mail address: bernardino.minana@gmail.com (B. Miñana).

PALABRAS CLAVE
Cáncer de próstata;
Castración;
Metástasis ósea;
Fractura;
Osteoporosis;
Osteopenia;
Bifosfonatos;
Anticuerpo monoclonal

Salud ósea en pacientes con cáncer de próstata

Resumen

Contexto: La salud ósea se ve comprometida en los pacientes con cáncer de próstata por la avanzada edad media al diagnóstico, los tratamientos de supresión androgénica y el desarrollo de metástasis óseas. Revisamos la literatura con la finalidad de actualizar el estado del arte sobre su incidencia, prevención y manejo.

Adquisición de la evidencia: Realizamos una revisión de la literatura sobre afectación ósea en los pacientes con cáncer de próstata en diferentes contextos clínicos.

Síntesis de la evidencia: Los pacientes diagnosticados de cáncer de próstata experimentan una disminución de la densidad mineral ósea mayor que varones de la misma edad antes de iniciar el tratamiento. La supresión androgénica provoca una pérdida de masa ósea más intensa durante el primer año de tratamiento, y parece ralentizarse a partir de entonces, persistiendo a largo plazo. Conocer del punto de partida y de la dinámica de la pérdida de masa ósea es importante para prevenir su progresión. Los eventos relacionados con el esqueleto ejercen gran impacto en la calidad de vida de los pacientes, y tanto el denosumab como el ácido zoledrónico han demostrado ser eficaces en su reducción.

Conclusiones: La prevención y el manejo de la afectación ósea en pacientes con cáncer de próstata es determinante para su calidad de vida y exige un abordaje individualizado. Antes de iniciar una supresión androgénica prolongada debe valorarse la situación de riesgo basal del hueso para adoptar las medidas protectoras apropiadas. En aquellos con metástasis debe considerarse precozmente el inicio de terapias que disminuyan el riesgo de eventos óseos.

Context

Prostate cancer (PCa) is the most frequent cancer among men and accounts for one of the most prevalent neoplasms in the Western world. According to data supplied by GLOBOCAN, the estimated incidence and mortality for 2008 in Europe were 94 new cases and 12 deaths per 100,000 men-year.[1] Data from the Spanish register 2010, on a sample of 21% of the population, give an estimated incidence rate of 82.27 per 100,000 men. Although around 4% of the patients with PC have metastases at diagnosis, nearly 40% will be eligible for androgen suppression therapy (AST) due to the presence of metastasis itself, as a concomitant therapy to radiotherapy or by complementing any previous radical treatment after biochemical recurrence.[2]

Bone, which is involved in over 80% of metastatic cases,[3] is the most frequent metastatic location for PCa. The main complications of these metastases (pain, spinal cord compression, fractures) add significant morbidity and a significant reduction in quality of life.

The significant number of patients who will receive prolonged AST, the advanced mean age, which is already a risk factor for the development of osteopenia or osteoporosis, and metastatic involvement are determinants of bone health care being crucial in the overall management of these patients.

Evidence acquisition

We conducted a review of the unstructured literature of those relevant published articles regarding the bone health of patients with PCa from a global perspective. To this end, we analyzed its impact on the different situations in which it is involved: at diagnosis, given the advanced mean age, as a result of AST and in a situation of bone metastasis.

Synthesis of the evidence

Hypogonadism and osteoporosis

In adults, a healthy bone is in a constant process of remodeling, with a balance between resorption and bone formation, mediated by the action of osteoblasts and osteoclasts, as well as numerous hormones, calcium levels, vitamin D, growth factors and cytokines, among others. Estrogens appear to be the determinant steroid hormone in the regulating process of bone resorption.[4] The testosterone that reaches the bone is converted into estrogens by aromatases. Therefore, hypogonadic males, whatever their origin, show marked estrogen deficiency, thus causing an imbalance in bone remodeling.[5]

Estrogen deficiency induces the production of proinflammatory cytokines such as TNF and IL 6 and the stimulation of the RANK and RANKL system, membrane ligands which activate osteoclast proliferation and differentiation from their precursor cells in the bone marrow.[6] Simultaneously, estrogen shortage blocks the transcription of osteoblast growth factors, which leads to a decrease in their activity and an increase in their apoptosis.

These factors condition a predominance of bone resorption, which results in a decreased bone mineral density that significantly increases the risk of fractures.

Osteoporosis associated with prostate cancer

Bone morbidity in patients with PCa is significant and is associated with epidemiological reasons, such as age,