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REVIEW

Hypofractionated radiation therapy versus conventional radiation therapy in prostate cancer: A systematic review of its safety and efficacy☆

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KEYWORDS
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Abstract
Context: New therapeutic alternatives can improve the safety and efficacy of prostate cancer treatment.
Objectives: To assess whether hypofractionated radiation therapy results in better safety and efficacy in the treatment of prostate cancer.
Acquisition of evidence: Systematic review of the literature through searches on PubMed, Cochrane Library, CRD, ClinicalTrials and EuroScan, collecting indicators of safety and efficacy.
Synthesis of the evidence: We included two systematic reviews and a clinical trial. In terms of efficacy, there is considerable heterogeneity among the studies, and no conclusive results were found concerning the superiority of the hypofractionated option over the normal fractionated option. In terms of safety, there were no significant differences in the onset of acute genitourinary complications between the two treatments. However, one of the reviews found more acute gastrointestinal complications in patients treated with hypofractionated radiation therapy. There were no significant differences in long-term complications based on the type of radiation therapy used, although the studies did have limitations.
Conclusions: To date, there are no conclusive results that show that hypofractionated radiation therapy is more effective or safer than normal fractionated radiation therapy in the treatment of localized prostate cancer.

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PALABRAS CLAVE
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Radioterapia hipofraccionada versus radioterapia convencional en cáncer de próstata: una revisión sistemática sobre eficacia y seguridad

Resumen
Contexto: Nuevas alternativas terapéuticas pueden mejorar la eficacia y seguridad del tratamiento del cáncer de próstata.
Objetivo: Evaluar si la radioterapia hipofraccionada conlleva mejor eficacia y seguridad en el tratamiento del cáncer de próstata.
Adquisición de la evidencia: Revisión sistemática de la literatura con búsqueda en Pubmed, Cochrane Libarry, CRD, ClinicalTrials y Euroscan, recogiéndose indicadores de efectividad y seguridad.
Síntesis de la evidencia: Se incluyeron 2 revisiones sistemáticas y un ensayo clínico. En relación con la eficacia existe una gran heterogeneidad entre los estudios, y no se encuentran resultados concluyentes de la superioridad de la opción hipofraccionada sobre la normofraccionada. En relación con la seguridad no se encuentran diferencias significativas en la aparición de complicaciones genitourinarias agudas entre ambos tratamientos. Sin embargo, una de las revisiones encuentra más complicaciones gastrointestinales agudas en los pacientes tratados con radioterapia hipofraccionada. En las complicaciones a largo plazo no se encuentran diferencias significativas según el tipo de radioterapia utilizada, aunque los estudios presentan limitaciones.
Conclusiones: Hasta el momento no existen resultados concluyentes que demuestren que la radioterapia hipofraccionada es más eficaz o segura que la normofraccionada en el tratamiento del cáncer de próstata localizado.

Introduction

Prostate cancer (PCa) is one of the main health problems in the male population. It is a rare malignancy in men younger than 50 years old, the age from which its incidence increases, with 90% of cases being detected in men over age 65. Its etiology is unclear, although we do know that it is associated with environmental exposures, lifestyles, a prior family history and genetic factors.[1,2]

In Spain, PCa ranks second in the general population, with an incidence of 12.9%, behind colorectal cancer (15%) and ahead of lung (12.4%) and breast tumors (11.7%). If we take into consideration the male population alone, the highest incidence corresponds to PCa (21.7%), followed by lung cancer (16.9%). The 5-year prevalence rate is also the highest one (31.4%) followed by colorectal cancer (16.4%).[3,4]

In absolute terms, cancer represents the first cause of death in Spain. PCa ranks fifth with respect to the general population with a mortality rate of 5.3%, behind lung (20.6%), colon and rectum (14.3%), breast (5.9%) and pancreas (5.6%) tumors. In males, mortality from PCa ranks third (8.6%) behind mortality caused by lung (27.4%) and colorectal (13.7%) tumors.[3,4]

PCa can be classified in different ways: according to tumor extent (TNM), histopathological grade (Gleason), clinical or histopathological stage and according to risk.[5–9] Once it has been diagnosed and the stage of the disease has been determined, there are several strategies for its clinical management, regarding initial treatment choice, the volume to be treated with radiotherapy (RT) if this therapeutic modality is chosen or clinical management after treatment. Any clinical-practice guideline on treatment of PCa includes information on the different treatment options depending on the clinical or pathological stage, with grades of evidence and recommendations in compliance with the criteria of the SIGN group.[10]

Treatment options, depending on the characteristics of each tumor, may range from expectant management of the disease to prostatectomy. RT is one of the major therapeutic pillars for clinically localized PCa, particularly external radiation therapy alone or in combination with androgen deprivation therapy.[7] However, optimal fractionation and total treatment time for PCa irradiation remain a matter of debate. It has been traditionally administered at fractions of around 1.8–2.0 Gy, 5 days a week for 8–9 weeks.[11,12] The total administered dose is usually 70–80 Gy.[12–15] In the past few decades, a new form of administering RT has emerged, hypofractionated RT, which is based on the delivery of higher doses per fraction during a smaller number of fractions, thus getting a lower total dose than in the case of RT with standard fractionation. In particular, hypofractionated RT in PCa involves administering a single-fraction radiation dose >2.1 Gy, 4 or 5 days a week, for 4–5 weeks. The total radiation dose in hypofractionated RT ranges between 52.5 and 72 Gy.[12–14,16]

The use of hypofractionated RT in PCa is justified by the fact that there is a dose–response relationship and a high sensitivity to the dose administered per fraction.[17,18] Hypofractionated RT could be more advantageous than conventional RT, since it would enable us to improve tumor control and to reduce radio-induced toxicity.[17] It could also offer other advantages, such as resource optimization, cost reduction and an improvement of the quality of life of the patient.[12,13,19] However, some studies have shown inconsistent findings regarding efficiency and safety when comparing both RT modalities, so an analysis of the available evidence