



## ORIGINAL ARTICLE

# Second neoplasm after treatment of localized prostate cancer<sup>☆</sup>

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### Abstract

**Introduction:** Prostate cancer (PC) treatment in early stages is radical prostatectomy (RP) or external radiotherapy (ER). There is some uncertainty regarding the development of new ER induced malignant tumors or second primary tumor (SPT), a fact influencing the choice of therapy. The purpose of this study is to determine the best therapeutic alternative for localized PC, in regards to incidence and time of development.

**Material and methods:** A systematic review of the literature is proposed by means of evaluation of studies conducted with localized PC and treated with RP or ER, published between 1990 and 2010. The Mega searchers used were Cochrane Library and Trip Database, and the databases used were MEDLINE, OVID, Science Direct, SciELO and LiLACS, using MeSH terms and free words. The studies selected were analyzed using the MINCIR score of methodological quality (MQ) to compare articles with different design. The variables were considered to be number of patients treated, localization of lesions, global incidence of STP and MQ of the studies. Averages, medians and weighted averages (WA) were calculated. The study groups were compared using the 95% confidence intervals of the medians.

**Results:** Eleven articles fulfilled the screening criteria (retrospective cohorts and case series); providing 13 series for the study. The average of MQ was 14.7 points (13 and 16 points). The most frequent localizations of STP were bladder, rectum and long. The WA of the global incidence of STP for the series was 3.6% (4.1% for ER and 2.2% RP).

**Conclusion:** The information existing did not make it possible to demonstrate an association between the appearance of STP and therapies for localized PC, even though there was a superior tendency in irradiated patients.

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**PALABRAS CLAVE**

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Segunda neoplasia;  
Revisión sistemática  
de la literatura

**Segunda neoplasia tras el tratamiento del cáncer prostático localizado****Resumen**

**Introducción:** El tratamiento del cáncer prostático (CP) en estadios precoces es la prostatectomía radical (PR) o la radioterapia externa (RE). Existe incertidumbre respecto del desarrollo de nuevos tumores malignos o segundo tumor primario (STP) inducidos por RE, hecho gravitante en la elección de la terapia. El objetivo de este estudio es determinar la mejor alternativa terapéutica para CP localizado, en lo que respecta a la incidencia y tiempo de desarrollo de STP.

**Material y método:** Se plantea una revisión sistemática de la literatura mediante la evaluación de estudios realizados con CP localizado y tratado con PR o RE, publicados entre 1990 y 2010. Se utilizaron los Mega buscadores Cochrane Library y Trip Database, y las bases de datos MEDLINE, OVID, Science Direct, SciELO y LiLACS, empleando términos MeSH y palabras libres. Los estudios seleccionados fueron analizados utilizando el score MINCIR de calidad metodológica (CM) para comparación de artículos con diferente diseño. Se consideraron las variables número de pacientes tratados, localización de lesiones, incidencia global de TSP y CM de los estudios. Se calcularon promedios, medianas y promedios ponderados (PP). Se compararon los grupos en estudio utilizando intervalos de confianza del 95% de las medianas.

**Resultados:** 11 artículos cumplieron los criterios de selección (cohortes retrospectivas y series de casos); aportando 13 series para el estudio. El promedio de CM fue 14,7 puntos (13 y 16 puntos). Las localizaciones más frecuentes de TSP fueron vejiga, recto y pulmón. El PP de la incidencia global de TSP para las series fue de 3,6% (4,1% para RE y 2,2% PR).

**Conclusión:** La información existente no permite demostrar asociación entre aparición de TSP y las terapias para CP localizado, a pesar de que existe una tendencia superior en pacientes irradiados.

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**Introduction**

Prostate cancer (PC) usually occurs in men over 50 years and has become more important worldwide due to the progressive increase in the incidence and mortality, constituting the fourth malignancy among men.<sup>1</sup> In Chile, the incidence of PC is unknown, but it has been estimated at 55–57 cases per 100,000 males.<sup>2</sup> In the meantime, mortality has experienced a permanent and progressive increase and now stands as the second leading cause of cancer death in men, with a mortality rate of 20.2 per 100,000.<sup>3</sup>

In localized stages (I and II), radical surgery is the standard treatment, external radiotherapy (ER) may also be performed, associated or not with hormone-blocking therapy. However, there is no conclusive evidence of the superiority in terms of survival of either technique. In recent years, brachytherapy has been incorporated as a therapeutic alternative.<sup>4,5</sup>

Radical prostatectomy (RP) is the complete removal of the prostate and the seminal vesicles. The most important complications are erectile dysfunction (29–100% of patients) and urinary incontinence, mild (4–50% of patients), and severe (0–15% of patients).<sup>5</sup> Currently, there are three types of ER (conventional, three-dimensional conformal, and of modulated intensity), and this evolution has made it possible to increase the doses with less damage to nearby tissues and organs.<sup>6,7</sup> The complications occur mainly at the level of the rectum and bladder, highlighting initially inflammatory problems and subsequently the atrophic and degenerative changes of neighboring tissues (anal, urethral stenosis, and fistula development).

There is some consensus that RP and ER are comparable in PC control,<sup>8</sup> even in terms of morbidity and quality of life one year after the treatment.<sup>8</sup> The high survival of PC in early stages has generated a new variable to consider, which are late complications among which is the possibility that ER can induce the occurrence of other tumors, known as second malignancy or second primary tumor (SPT).<sup>9,10</sup>

A latency period of at least 5 years is accepted for the development of radiation-induced SPT.<sup>11</sup> It is also accepted that variables such as patient's age, the target organ, the dose used, the extent of irradiated tissue, and the type of radiotherapy are crucial to its development.<sup>12</sup> However, the incidence of radiation-induced tumors was underestimated because of the short survival associated with the old radiotherapy; but, with the technological advancement, there have been substantial improvements in survival with radiotherapy that usually exceed 15 years or more. This has allowed us to quantify a cumulative incidence of SPT of up to 20%.<sup>12</sup>

There are currently at least three narrative reviews related to the subject,<sup>12–14</sup> which include the personal view of the author or authors regarding the situation, although there is no systematic review to summarize and organize the available evidence regarding this uncertainty. The objective of this study is to determine the best therapeutic option for patients with localized PC (RP or ER), in terms of incidence and time of development of SPT. The methodology of this manuscript was based on the PRISMA initiative for conducting systematic reviews and meta-analyses.<sup>15–17</sup>

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