



## ORIGINAL ARTICLE

## Hormonal changes after localized prostate cancer treatment. Comparison between external beam radiation therapy and radical prostatectomy<sup>☆</sup>

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### KEYWORDS

Prostate cancer;  
Radiotherapy;  
Radical  
prostatectomy;  
Gonadotrophin;  
Testosterone

### Abstract

**Objective:** To determine the influence of radical prostatectomy (RP) and external beam radiation therapy (EBRT) on the hypothalamic pituitary axis of 120 men with clinically localized prostate cancer treated with RP or EBRT exclusively.

**Materials and methods:** 120 patients with localized prostate cancer were enrolled. Ninety-two patients underwent RP and 28 patients EBRT exclusively. We measured serum levels of luteinizing hormone, follicle stimulating hormone (FSH), total testosterone (T), free testosterone, and estradiol at baseline and at 3 and 12 months after treatment completion.

**Results:** Patients undergoing RP were younger and presented a higher prostate volume (64.3 vs. 71.1 years,  $p < 0.0001$  and 55.1 vs. 36.5 g,  $p < 0.0001$ ; respectively). No differences regarding serum hormonal levels were found at baseline. Luteinizing hormone and FSH levels were significantly higher in those patients treated with EBRT at three months (luteinizing hormone 8.54 vs. 4.76 U/l, FSH 22.96 vs. 8.18 U/l,  $p < 0.0001$ ) while T and free testosterone levels were significantly lower (T 360.3 vs. 41,483 ng/dl,  $p 0.039$ ; free testosterone 5.94 vs. 7.5 pg/ml,  $p 0.018$ ). At 12 months FSH levels remained significantly higher in patients treated with EBRT compared to patients treated with RP (21.01 vs. 8.51 U/l,  $p < 0.001$ ) while T levels remained significantly lower (33,989 vs. 40,239 ng/dl,  $p 0.03$ ).

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**PALABRAS CLAVE**

Cáncer de próstata;  
Radioterapia;  
Prostatectomía  
radical;  
Gonadotropina;  
Testosterona

**Conclusions:** Prostate cancer treatment influences the hypothalamic pituitary axis. This influence seems to be more important when patients with prostate cancer are treated with EBRT rather than RP.

More studies are needed to elucidate the role that prostate may play as an endocrine organ.  
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### Cambios hormonales después del tratamiento de cáncer de próstata localizado. Comparación entre radioterapia de haz externo y prostatectomía radical

**Resumen**

**Objetivos:** Determinar la influencia de la prostatectomía radical (PR) y de la radioterapia externa (RT) sobre el eje hipotálamo-hipofisario de 120 pacientes con cáncer de próstata clínicamente localizado tratados con PR o RT exclusiva.

**Material y métodos:** Estudiamos 120 pacientes con cáncer de próstata localizado. Noventa y dos pacientes recibieron PR y 28 RT exclusiva. Medimos los niveles séricos de hormona luteinizante, hormona folículo estimulante (FSH), testosterona total (T), testosterona libre y estradiol basalmente y a los 3 y 12 meses tras completar el tratamiento.

**Resultados:** Los pacientes sometidos a PR eran más jóvenes y presentaban mayor volumen prostático (64,3 vs. 71,1 años,  $p < 0,0001$  y 55,1 vs. 36,5 g,  $p < 0,0001$ ; respectivamente). No encontramos diferencias en los niveles hormonales basales. Los niveles de hormona luteinizante y FSH eran significativamente superiores en los pacientes tratados con RT a los 3 meses (hormona luteinizante 8,54 vs. 4,76 U/l, FSH 22,96 vs. 8,18 U/l,  $p < 0,0001$ ) y los niveles de T y testosterona libre significativamente inferiores (T 360,3 vs. 414,83 ng/dl,  $p 0,039$ ; FT 5,94 vs. 7,5 pg/ml,  $p 0,018$ ). A los 12 meses los niveles de FSH permanecían significativamente superiores en los pacientes tratados con RT comparado con pacientes tratados con PR (21,01 vs. 8,51 U/l,  $p < 0,001$ ) y los niveles de T permanecían significativamente inferiores (339,89 vs. 402,39 ng/dl,  $p 0,03$ ).

**Conclusiones:** El tratamiento del cáncer de próstata influye en el eje hipotálamo-hipofisario. La influencia parece más importante en los pacientes tratados con RT.

Necesitamos más estudios que eluciden el papel que la próstata puede jugar como órgano endocrino.

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**Introduction**

In males, testosterone is synthesized primarily in Leydig cells. The number of Leydig cells is in turn regulated by the luteinizing hormone (LH) and follicle-stimulating hormone (FSH). The amount of testosterone synthesized is regulated by the hypothalamic-pituitary-testicular axis. When testosterone levels are low, the gonadotropin-releasing hormone (GnRH) is released by the hypothalamus, which in turn stimulates the pituitary gland to release FSH and LH. The latter two hormones stimulate the testis to synthesize testosterone.

Several studies have evaluated the changes in the levels of gonadotropins and testosterone following radical prostatectomy (RP)<sup>1-5</sup> or external beam radiation therapy (EBRT)<sup>6-11</sup> in patients with clinically localized prostate cancer. A trend toward a compensated hypergonadotropic hypogonadism has been reported after the removal of the whole prostate gland as well as after prostate radiotherapy, but results are not consistent. Despite the data obtained from these studies, little is known concerning the role that the prostate may play as an endocrine organ and its influence on the hypothalamic-pituitary-gonadal axis.

Different psychological and organic theories have been postulated in order to explain the reduction of testicular production of testosterone after RP. The psychological stress of facing a cancer diagnosis or the fear of surgery have already been considered potential causes of the suppression of the luteinizing hormone/follicle stimulating hormone (LH/FSH) prior to RP.<sup>4</sup> Organic factors, like the ligation of Santorini's venous plexus or of prostatic vascular pedicles and the Trendelenburg position, may theoretically cause transient ischemic or hypoxic damage to the testicles. Moreover, damage to the cavernous nerves may alter the testicular function in humans, as it has been reported in animal models.<sup>12</sup> Other studies have reported that the prostate produces two substances that may influence the feedback regulation of gonadotropins; dihydrotestosterone (DHT) and inhibin, a glycoprotein produced in the testis and prostate, which inhibits the production and/or secretion of pituitary gonadotropins, preferentially FSH.<sup>13-15</sup>

On the other hand, a decline in the patient's serum testosterone level after EBRT for prostate cancer has been described. Due to anatomic proximity, it has been hypothesized that scattered radiation to the Leydig cells of the testes from pelvic EBRT would be correlated with decreased

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