



ORIGINAL ARTICLE

Influential factors in the response to salvage radiotherapy after radical prostatectomy[☆]



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Abstract

Objective: To analyze the influential factors in the response in prostatectomized patients with subsequent biochemical relapse (BCR) and treated with salvage radiotherapy (RTP).

Materials and methods: We analyzed 313 patients with pT2/pT3 prostate cancer who were receiving salvage therapy due to biochemical relapse (from a series of 1310 radical prostatectomies between 1989 and 2012). Of the 313 patients, 159 (50.8%) only received androgen deprivation (AD), 63 (20.1%) radiotherapy (RTP) plus concomitant AD and 91 (29.1%) only RTP. Of these, 57 (62.6%) have maintained complete response and 34 (37.4%) had failure response with post-RTP BCR.

Results: Study of the group treated exclusively with salvage RTP. Ninety-one patients were treated with salvage RTP. Median follow-up was 6.4 years and median to recurrence 11 months. Post-RTP biochemical relapse-free survival (PRBRFS) was $68 \pm 7\%$ and $30 \pm 10\%$ in 5–10 years. Median PRBRFS was 7.3 years (6.3–8.3). Initial PSA (HR: 1.08; 95% CI: 1.01–1.1 $P=0.02$) with best PSA cut-off point $PSA > 20$ ng/ml (HR: 13.6; 95% CI: 2.1–86 $P=0.005$) and PSA pre-RTP (HR: 1.9; 95% CI: 1.2–3.3; $P=0.009$), best PSA cut-off point $PSA \text{ preRTP } 0.92$ ng/ml (HR: 4.5; 95% CI: 1.3–15.6; $P=0.01$) showed independent influence in the response in the multivariate study. PRBRFS at 5 years was $81 \pm 9\%$ versus $58 \pm 9\%$ with initial $PSA < 20$ or > 20 ng/ml ($P=0.03$). PRBRFS at 5 years was $93 \pm 5\%$ versus $53 \pm 10\%$ according to $PSA \text{ pre-RTP } < 0.9$ or > 0.9 ng/ml ($P=0.02$).

Conclusions: In patients treated with salvage RTP after radical prostatectomy, the preoperative $PSA > 20$ ng/ml and $PSA \text{ preRTP } > 0.92$ ng/ml show an independent influence on the response.

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PALABRAS CLAVE

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Factores influyentes en la respuesta al rescate con radioterapia tras prostatectomía radical**Resumen**

Objetivo: Analizar en los pacientes prostatectomizados con posterior progresión bioquímica (PB) y tratados con radioterapia de rescate (RTP) los factores influyentes en la respuesta.

Material y métodos: Analizamos 313 pacientes con cáncer de próstata pT2/pT3 que reciben tratamiento de rescate por PB (de una serie de 1.310 pacientes operados entre 1989-2012). De los 313 pacientes 159 (50,8%) reciben solo deprivación androgénica (DA), 63 (20,1%) radioterapia (RTP) más DA concomitante y 91 (29,1%) solo RTP, de los cuales 57 (62,6%) mantienen respuesta completa y 34 (37,4%) fracaso del tratamiento.

Resultados: Estudio del grupo tratado solo con RTP de rescate: 91 pacientes son tratados con RTP de rescate. Mediana de seguimiento 6,4 años. Mediana hasta progresión 11 meses. La supervivencia libre de progresión bioquímica post-RTP (SLPBPR) es de $68 \pm 7\%$ y $30 \pm 10\%$ en 5 y 10 años y la mediana de SLPBPR 7,3 años (6,3-8,3). En el análisis multivariado presentan influencia independiente en la respuesta: el PSA inicial (HR: 1,08; IC 95%: 1,01-1,1; $p=0,02$) con mejor punto de corte PSA > 20 ng/ml (HR: 13,6; IC 95%: 2,1-86; $p=0,005$) y PSA pre-RTP (HR: 1,9; IC 95%: 1,2-3,3 $p=0,009$), mejor punto de corte PSA preRTP de 0,92 ng/ml (HR: 4,5; IC95% 1,3-15,6; $p=0,01$). SLPBPR a 5 años $81 \pm 9\%$ frente a $58 \pm 9\%$ con PSA inicial < 20 o > 20 ng/ml ($p=0,03$). SLPBPR a 5 años $93 \pm 5\%$ frente a $53 \pm 10\%$ según PSA pre-RTP $< 0,9$ o $> 0,9$ ng/ml ($p=0,02$).

Conclusiones: En los pacientes prostatectomizados tratados con RTP de rescate el PSA preoperatorio > 20 ng/ml y el PSA preRTP $> 0,92$ ng/ml tienen influencia independiente en la respuesta.

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Introduction

Between 15 and 40% of patients treated with radical prostatectomy show biochemical progression (BP) in time.¹ The indication for salvage radiotherapy (RTP) in patients treated with surgery is a much-discussed topic. Only in English more than 200 articles have been published since 1990. Regrettably, the general attitude is still relatively reluctant. It is estimated that 50% of urologists remain watchful waiting, 30% indicate salvage with androgen deprivation (AD) and the rest with RTP.²

Among the various treatment options with RTP, it is the only potentially curative option.³ However, 10–61% of the irradiated ones show post-RTP BP⁴⁻⁷ due to treatment failure. It is essential to know the influential clinicopathologic factors in radiotherapy failure.^{4,8} The therapeutic approach is largely dependent on this knowledge in patients operated with BP.

Most published studies belong to the Anglo-Saxon world, with probably different connotations to ours. Thus, the objective of this study is to evaluate the factors influencing the response in patients undergoing radical prostatectomy with subsequent BP and treated with salvage RTP.

Materials and methods

We retrospectively analyzed 313 patients with pT2-pT3 prostate cancer (from a series of 1310) operated between January 1989 and December 2012 and receiving salvage treatment due to BP.

Before surgery, every patient underwent a detailed clinical history with physical examination (including DRE), PSA, and prostate biopsy. The study was completed with computed tomography till July 2000. Since then we have preferably used MRI (729 patients) without following special criteria, since the original purpose was to assess its diagnostic efficacy.

Until 2000, bone scan was performed in all patients, and from then onwards only to patients with PSA greater than 20 ng/ml and/or Gleason > 6 . In all cases radical retropubic prostatectomy modified according to the technique described by Walsh⁹ in 1982 was performed, with systematic bilateral ilio-obturator lymphadenectomy until 2007, and then in the case of having a PSA greater than 15 ng/ml, clinical Gleason equal to or greater than 7, or a clinical stage T2b, was performed. The laparoscopic approach was performed in our center for the first time in 2005.

Examination of the pieces was carried out by 2 expert pathologists devoted to urological disease according to the technique described by True.¹⁰ We have also studied the expression of Ki67. In 2000 we revealed the relationship of Ki67 with a worse stage and prognosis of the disease.¹¹ We would like to study whether this trend is maintained in patients treated with RTP. Since then the determination of Ki67 was performed in 380 patients without following special criteria, since its initial aim was to assess its prognostic efficacy. All the immunohistochemical analyses were performed on sections of 4 micromeres fixed in formalin and obtained from the paraffin-embedded primary tumor. The result was expressed in percentage of stained cells.

After surgery, the analytical follow-up was performed by means of PSA determinations at 3, 6, and 12 months

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