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Artigos de Revisão

PSA following prostate brachytherapy (^{125}Iodine) without hormonotherapy or external beam radiation

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Resumo

Objectivo: Apresentar a uma revisão da literatura sobre a interpretação do PSA após a braquiterapia com ^{125}I.

Material e métodos: Procedeu-se a uma pesquisa de "medline" sobre o doseamento de PSA após a braquiterapia, "PSA bounce", "PSA spike", falência bioquímica e recorrência de carcinoma da próstata após braquiterapia.

Resultados: A definição de falência bioquímica após braquiterapia (ASTRO) não é sinónimo de falência clínica. Cerca de 30% dos doentes submetidos a braquiterapia desenvolvem "PSA bounce" cuja etiologia é desconhecida. "PSA bounce" ocorre mais frequentemente no 1º e 2º ano após o implante.

Há casos de doentes em que o PSA elevado e a biópsia persistentemente positiva apresentam diminuição subsequente de PSA para valores consistentes com erradicação do carcinoma da próstata não necessitando de tratamento de salvação.

Conclusões: O diagnóstico de recorrência de carcinoma da próstata após a braquiterapia mantém-se controverso.

O "PSA bounce" ocorre frequentemente. A definição da ASTRO de falência bioquímica não é equivalente a falência clínica nem é justificação para terapêutica de salvação.

Os doentes e seus médicos devem ser pacientes e não se precipitarem em instituir terapêuticas de salvação muitas vezes desnecessárias e associadas a morbilidade importante.

Palavras chave: Carcinoma da próstata; Braquiterapia; Antigénio Específico da Próstata

Abstract

Purpose: Review of PSA interpretation after prostate brachytherapy (^{125}I).

Material and Methods: Medline research about PSA following prostate brachytherapy, PSA bounce, PSA spike, Biochemical failure and prostate cancer recurrence after prostate brachytherapy.

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Results: Astro definition of biochemical failure is not equivalent of clinical failure. About 30% of implant patients develop PSA bounce. The etiology is unknown. PSA bounce is frequent during the first and second years after the implant.
Cases are reported with elevated PSA and positive prostate biopsies which on subsequently follow up the PSA falls to values consistent to cancer control.
Conclusion: Recurrence of prostate cancer diagnosis following prostate brachytherapy remains controversial. PSA bounce occurs very often. Astro definition of biochemical failure is not equivalent to clinical failure and is not justification to salvage treatment. Patients and Doctors should not rush to salvage treatment which could be unnecessary and has high morbidity.

Key-words: Prostate cancer; Brachytherapy; Prostate Specific Antigene

Modern Prostate brachytherapy is an accepted treatment of localised prostate cancer. It is very attractive because of its low morbidity and shorter inactivity time. It can be performed as an outpatient procedure.

Prostate-specific antigen (PSA) determination is used to monitor patients after the implant. However the interpretation of PSA results can become confusing for both patients and doctors.

Unlike radical prostatectomy, the PSA after brachytherapy falls slowly taking several months, even years to achieve a nadir value. This is due to 125I half-life of 60 days; it takes 180 days to deliver almost 90% of the entire dose.

On the other hand, PSA can intermittently rise and fall during several years after the implant due to PSA release from partially damaged normal prostatic epithelium and the long time lethally damaged cancer cells take to die and stop producing PSA.

The American Society for Therapeutic Radiology and Oncology (ASTRO) defined biochemical failure as three consecutive elevations of PSA to signal failure. The date of failure should be the mid-point between the post-irradiation nadir PSA and the first of the three consecutive rises (2).

However the sameASTRO consensus statement argues that biochemical failure is not equivalent to clinical failure and in most cases do not justify therapeutic intervention.

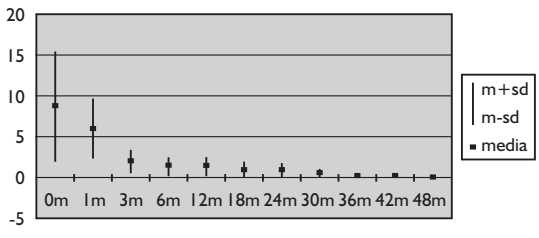

Fig. 1 – Lisbon Proseed Series: PSA following ^{125}I brachytherapy monotherapy in 204 patients (1)

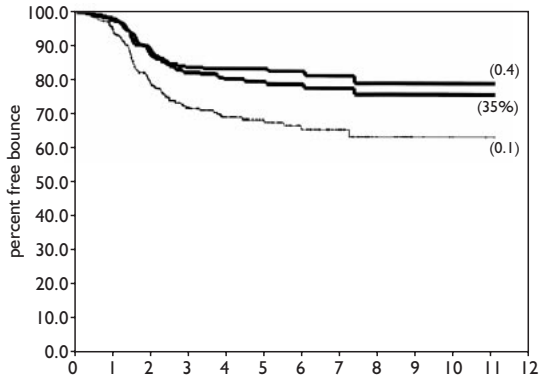

Fig. 2 - Freedom from developing a PSA Bounce using three different definitions: >0.1 ng/ml, > 0.4 ng/ml and > 35% (3).

About 30% of implant patients have a moderate, temporary PSA rise between 1 and 3 years after brachytherapy witch is referred as a PSA bounce or PSA spike(3). Most of these patients experience subsequent normalization of PSA without treatment.

The etiology of PSA bounce is unknown. Radiation prostatitis by compromising membrane integrity in PSA-producing prostate epithelium may be an answer.

Various definitions of PSA bounce have been used: It could be a rise of 0.1 ng/ml(4), 0.2 ng/ml(5) or even 0.4ng/ml(6). Others propose a rise of more than 35% from the baseline prior value(7).

Figure 2 shows the incidence of PSA bounce using three different definitions (>0.1 ng/ml, >0.4 ng/ml and >35%) as calculated by Stock et al (3).

Figure 3 shows the time to develop a PSA bounce using the same three definitions. The majority of the patients that develop a PSA bounce experience this during 1 and 2 years after the implant. However, about

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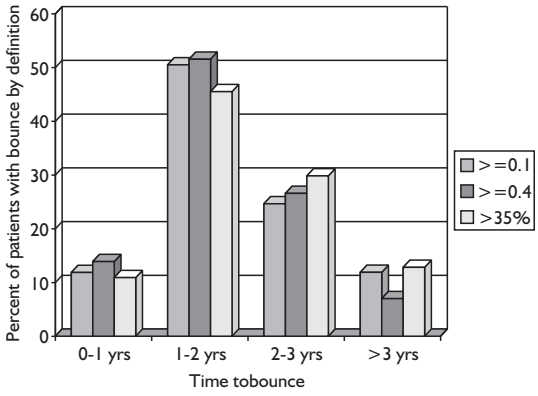

Fig. 3 – Time to develop a PSA bounce (3)

10% of them experience a PSA bounce even more than 3 years after the implant.

Merrick et al (8) analysed PSA kinetics in patients with and without a spike. PSA spikes developed at approximately 18 months in patients with one or multiple spikes. Despite differences in the PSA kinetics, the PSA curves converged at approximately 66 months. For men with a follow-up longer than 66 months, the mean PSA level for patients with or without spikes was less than 0.1 ng/ml.

Reed et al (9) showed that transient PSA rises can even occur in the presence of a persistently positive biopsy. On subsequently follow up the PSA fall to values consistent to cancer control.

Reed et al reported 8 low risk patients witch had been implanted with 125 I brachytherapy without hormonotherapy or external beam radiation. Post implant biopsies were performed because a persistently elevated PSA level. Despite biopsies were positive the patients were left without any treatment. Follow-up from implantation ranged from 39 months to 91 months (median 58). Follow up after PSA spike ranged from 12 to 72 months (median 39). Patients last PSA values ranged from 0.1 to 0.5 ng/ml (median 0.2).

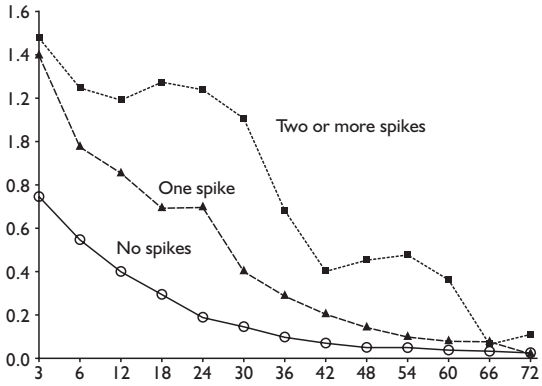

Fig. 4 – PSA kinetics following prostate brachytherapy (8)

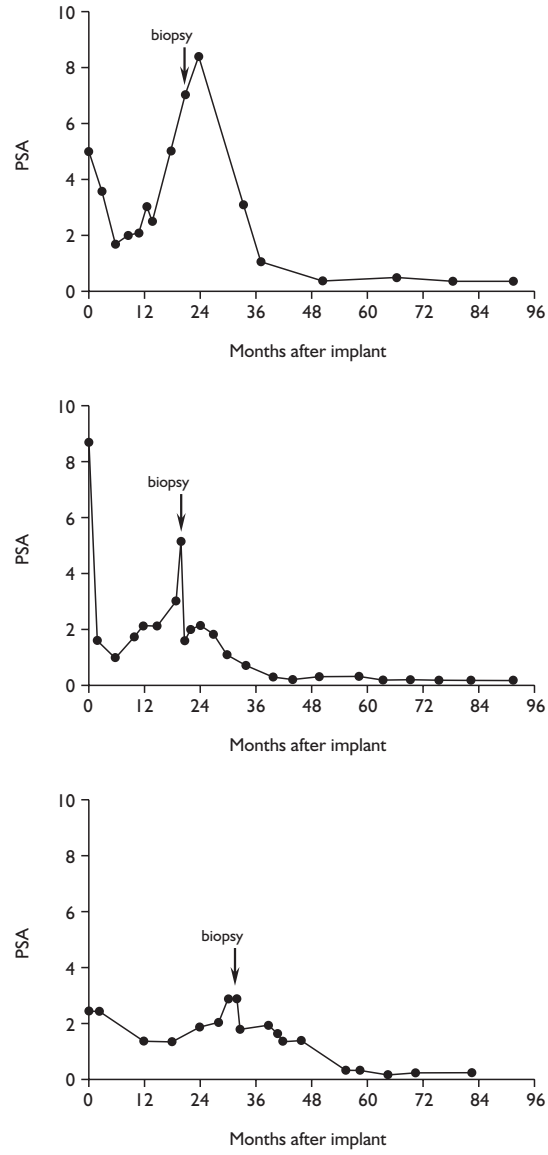

Fig. 5 – Case histories of PSA spikes and positive biopsies after prostate brachytherapy (9)

It is well known that postimplant biopsies commonly convert from positive to negative with additional follow-up because of slow cancer involution.

Reeds conclusion is that PSA spikes up to 10 ng/ml is still consistent with cancer eradication. Transient PSA rises can even occur in the presence of a positive biopsy. He advises not to rush ahead with salvage therapy.

The difficulty is to differentiate between a PSA bounce and a true cancer recurrence.

Pretreatment prognostic factors as the Gleason score, PSA and clinical stage and the implant quality defined by the D90 are related to treatment failures and are probably the best clues to diagnose a cancer recurrence (10).

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PSA velocity should suggest local versus systemic recurrence: Zaggars et al (11) found that patients with a PSA doubling time exceeding 8 months had only 7% metastasis rate. D'Amico et al (12) showed that patients with a PSA doubling time less than 12 months had a very high prostate cancer specific death.

Conclusion

The diagnosis of localised prostate cancer recurrence after prostate brachytherapy remains controversial.

PSA bounce occurs very often. ASTRO definition of biochemical failure is not equivalent of clinical failure or justification to salvage therapy.

Patients and doctors should be patient and must balance the need to cure and high morbidity of salvage therapies.

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