The optimal time for the first PSA evaluation post radical prostatectomy

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Abstract

Introduction and objectives: Although an imperfect tool for prostate cancer screening, the PSA remains important in monitoring disease recurrence after primary prostate cancer treatment and subsequent therapies. The serum half life of the PSA ranges between 2 and 3 days so this marker should be undetectable in 3-4 weeks after radical prostatectomy (RP). There is no general consensus regarding the moment in time on which the first PSA value should be obtained after RP, intervals varying between 4 and 12 weeks. The aim of this paper is to determine the earliest PSA valid result after prostatectomy, which is important in patients who need further adjuvant therapies (radiation and/or hormonal).

Materials and methods: During 3 years (2010 – 2013), 324 prostatectomies were performed in our center, of which 176 were patients with high risk prostate cancer, where the post prostatectomy PSA value has a very important role (PSA persistence / PSA recurrence) in further treatment strategies. The study was conducted on 78 patients, that had their postoperative serum PSA dosed at 4, 6, and 12 weeks respectively, and afterwards every 3 months. An ultra sensitive PSA assay was used in all cases (0.003 ng/ml detection limit).

Results: In a number of 21 patients (26.9%) the PSA value obtained at 4 weeks post RP was higher than the detection limit (median 0.05 ng/ml) and dropped under the detection limit at 6 weeks, remaining there for the rest of the study period, requiring no further treatment. In 16 patients (20.5%) the PSA value was undetectable at 4 weeks. For 41 patients (52.6%) the value at 4 weeks was above the detection limit, and raised during the study period. These patients were referred for further therapies (salvage radiotherapy and/or continuous ADT) in concordance with clinical and histopathological features.

Conclusions: 4 weeks is not enough time for the complete PSA clearance in all patients, as mentioned in the literature. 6 weeks was the appropriate time for a valid PSA result post RP, with an important role in the therapeutic sequence, especially in high risk and very high risk groups of prostate cancer patients.

Keywords: PSA; Radical prostatectomy; ultra sensitive PSA assay
Clinical studies

Introduction and objectives

From its early discovery in 1979 by Dr. Ming C. Wang, the PSA represented a valuable tool for the urologist and although its role in prostate cancer (PC) screening is debatable in the scientific literature right now, its role in patient surveillance post PC treatment remains unquestionable.

The PSA, known as human kalikrein 3 (hK3) is a protease originated in the prostate epithelium. Normally minimal quantities of PSA are released in the blood flow.

In a patient with Prostate Cancer the abnormal level of PSA in the blood flow is obtained by increase prostate outflow rather than increased production.

When it is released, the PSA has 2 major forms: an active one, which will circulate in the blood flow combined with a protease inhibitor (cPSA) and an inactive one which travels free in the blood flow (fPSA). The free PSA has three variable forms: inactive PSA (iPSA), benign PSA (bPSA) and one represented by variable precursor forms of PSA (pPSA)³, ⁴.

As a screening tool PSA lacks good specificity, especially in low PSA values. The usual cut-off value set for biopsy indication is 4ng/ml, but there are studies which show that by choosing this value limit for biopsy between 20-40% of PC are not diagnosed ⁵, ⁶.

Through time the detection limit of PSA tests evolved and became lower. At the current time ultra sensitive tests can detect PSA levels of < 0.1 ng/ml.

The serum half life of the PSA ranges between 2 and 3 days⁷ so this marker should be undetectable in 3-4 weeks after radical prostatectomy (RP).

An undetectable PSA post-radical prostatectomy (RP) represents a favorable prognosis factor, with consistent smaller percentage of biochemical recurrence at 5 years⁸.

Regarding the timing of first PSA post RP there is no general consensus, with intervals varying widely between 4 and 12 weeks.

For this purpose we conducted our study to determine the optimal timing for the first PSA value post RP, with great importance in our opinion, especially in patients with high risk PC who may benefit from further adjuvant treatment.

Materials and methods

In the last 3 years (2010 – 2013), 324 radical prostatectomies (RP) were performed in our center from which 176 were patients with high risk prostate cancer (Img. 1).

Our study was conducted on 78 patients who underwent a RP for PC, all of which were ranked as part of the high risk PC group, according to the D’Amico criteria (PSA > 20 ng/mL, or GS > 7, or TNM ≥ cT2C)⁹.

They all underwent a standard retropubic prostatectomy, combined with an extended lymph node dissection.

The study protocol consisted in a series of post-operative measurements of serum PSA at 4, 6, and 12 weeks after RP.

If no further adjuvant therapy was indicated based on the postoperative PSA values the patients entered a follow-up scheme consisting in periodical 3 month PSA testing.

In all cases we used an ultra sensitive PSA assay (0.003 ng/ml detection limit) in order to obtain accurate and valid results for the whole study group.

Results

In 16 patients (20.5%) the PSA value was undetectable at 4 weeks post RP (Img. 2).

In a number of 21 patients (26.9%) the PSA value obtained at 4 weeks post RP was higher than the detection limit (median 0.05 ng/ml) and dropped under the detection limit at 6 weeks, remaining there for the rest of the study period.

![Img. 2 PSA Status of the study group at 4 weeks post RP](image-url)
Clinical studies

These patients received no further treatment and were placed in a follow-up program consisting in a serum PSA evaluation at every 3 months.

For 41 patients (52.6%) the value at 4 weeks was above the detection limit, and raised during the study period. (Img. 3)

These patients were referred for further therapies (salvage radiotherapy and/or continuous ADT) in concordance with clinical and histopathological features.

In our patients’ data there was no variation of the PSA value between the determinations at 6 and 12 weeks (Img. 4, 5).

Discussions

It is estimated that between 25-32% of all patients who undergo a prostatectomy will eventually experience BCR, this percent rising to > 50% in the high risk PC groups10.

But biochemical recurrence (BCR) is a notion that is not as well defined in patients who undergo radical prostatectomy as it is for patients who undergo external beam radiotherapy9.

There are currently several definitions based on different PSA cut off values, the most widely accepted definition being the one which defines BCR as 2 successive PSA values > 0.2 ng/ml.

The BCR problem becomes more complicated, because there are studies who state that this threshold can be lowered to two subsequent rises > 0.1 ng/ml or even ≥ 0.05 ng/ml in patients with high risk of PC locally advanced disease (Gleason score 8-10; T3b; N+)12.

The whole concept of detecting the BCR in a shorter time after the surgery is tremendously important because as current data in the literature suggest the faster we start a salvage radiotherapy regime in a patient who needs one, the more benefit he has in terms of PSA control, advancement to systemic disease and PC mortality13.

At current time there are no clear evidences regarding prolonged survival in favor of adjuvant radiotherapy (in patients with high risk of PC local recurrence) or salvage radiotherapy (performed only in patients with BCR)14.

Our current opinion is in favor of an early started salvage radiotherapy rather than adjuvant radiotherapy, in order to protect patients from radiation side effects and to deliver this treatment only to patients who may benefit from it.

Even in high risk PC patients there is an estimate that between 35-76 % are alive and cancer free at 10 years, after RP alone15, so great care must be taken not to over-treat these patients.

If the serum PSA half-life is considered to be between 2 and 3 days, an interval of time near 30 days should be enough for complete PSA clearance but according to our study data it seems that the optimal interval for a valid first PSA measurement post RP would be 6 weeks.

Based on our study data in the high risk PC, an optimal management post RP needs a reliable first PSA value, and for this we believe that 6 weeks is the earliest time at which a valid result can be obtained.

Conclusions

In our studied group 4 weeks was not enough time for complete PSA clearance in all patients, as mentioned in the literature; 6 weeks was the appropriate time for a valid PSA result post RP.

This first PSA value has an important role in the
therapeutic sequence, especially in high risk and very high risk groups of prostate cancer patients.

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