Asian Journal of Urology (2016) 3, 59–63

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajur

ASIAN FOCUS

Prostate specific antigen bounce after intensity-modulated radiation therapy in an Asian population

Yu Guang Tan [a*], Weber Lau Kam On [a], Hong Hong Huang [a], Terence Tan Wee Kiat [b]

[a] *Department of Urology, Singapore General Hospital, Singapore*
[b] *Department of Radiotherapy, National Cancer Centre Singapore, Singapore*

Received 19 August 2015; received in revised form 30 November 2015; accepted 8 December 2015
Available online 13 January 2016

KEYWORDS
Prostate specific antigen;
Prostate specific antigen bounce;
Prostate cancer;
Intensity modulated radiation therapy

Abstract *Objective:* Serum prostate specific antigen (PSA) is commonly used to evaluate treatment response after definitive radiation therapy (RT). However, PSA levels can temporarily rise without a clear reason, termed "PSA bounce", and often engender great anxiety for both patients and physicians. The present study aimed to determine the prevalence and factors that predict "PSA bounce" after intensity-modulated radiation therapy (IMRT), and the relevance to biochemical failure and cancer recurrence in an Asian population.
Methods: We retrospectively reviewed 206 patients who received IMRT for prostate cancer from 2004 to 2012 in the National Cancer Centre Singapore. These patients were followed up with regular PSA monitoring. We defined "PSA bounce" as a rise of 0.1 ng/mL, followed by two consecutive falls. Patients with biochemical failure (PSA nadir + 2 ng/mL) were further evaluated for cancer recurrence.
Results: Sixty-one patients (29.6%) experienced "PSA bounce", at a median time of 16 months and lasted for 12 months. Age remained the most consistent predictor of the incidence, duration and extent of "PSA bounce". Other contributory factors included baseline PSA, Gleason score and PSA nadir. Hormonal therapy and prostate volume did not affect this phenomenon. Sixteen patients (7.8%) developed biochemical recurrence, at median time of 32 months, of which 11 were confirmed to have metastatic disease. The median follow-up time was 71 months.

* Corresponding author.
E-mail address: yuguangtan90@gmail.com (Y.G. Tan).
Peer review under responsibility of Second Military Medical University.

http://dx.doi.org/10.1016/j.ajur.2015.12.001

Conclusion: A younger age predicts PSA bounce incidence, duration and magnitude. The extent of bounce appears to be lower in Asian population. The interval to occurrence and extent of PSA elevation separates PSA bounce from disease recurrence.

1. Introduction

Serum prostate specific antigen (PSA) is a sensitive measure of treatment outcome for prostate cancer [1]. Although undetectable levels can be expected after a few weeks for patients undergoing radical prostatectomy, it can take 2–5 years to achieve a nadir PSA level with radiation therapy (RT), owing to the slower process of tumor-cell killing [2]. More importantly, it is not uncommon for the PSA levels to rise temporarily, a phenomenon known as "PSA bounce" [3,4], first described by Wallner and colleagues in 1997 [5]. While the exact etiology remains unknown, it is hypothesized to be the result of prostate cell membrane instability, bacterial and radiation prostatitis [6]. Although the relevance to biochemical failure remains controversial, these fluctuations can engender much anxiety amongst the physicians and patients.

The present study is the first to examine PSA bounce after intensity modulated radiation therapy (IMRT) in an Asian population. In particular, we reviewed the factors associated with this phenomenon, in order to stratify the patient profile that will most likely present with a PSA bounce. We also looked at the relevance to biochemical failure and synthesized an approach to help physicians differentiate between the two entities.

2. Patients and methods

We retrospectively reviewed 206 consecutive patients that received IMRT for prostate cancer from 2004 to 2012 at the National Cancer Centre Singapore. Data were obtained from review of casenotes, cancer registry and electronic records with IRB approval from the Singhealth Ethics Committee. None of the patients had nodal or metastatic spread prior to treatment. A variety of factors were recorded, including the patients profile, cancer staging and risk group, the concomitant use of androgen deprivation, the onset, magnitude and duration of PSA bounce and the time to biochemical failure. External radiotherapy was delivered via IMRT, planning for at least 90% of the planning target volume to receive the prescribed dose (of 70 to 74 Gy).

Given the retrospective nature of this study, follow-ups were not consistently standardized. However, in our institution's follow-up protocol, we recommended quarterly for the first 2 years post-operatively, semiannually for the subsequent 3 years and yearly follow-ups onwards. PSA level and digital rectal examination were done routinely at follow-ups. We defined PSA bounce as a rise of 0.1 ng/mL, followed by two consecutive falls. Biochemical failure was defined according to the Phoenix criteria, a rise of 2 ng/mL above nadir.

Patients with biochemical failure were all further evaluated with imaging and bone scan to detect any disease recurrence.

Statistical analyses were performed using SPSS statistics version 21.0 (IBM, New York, USA). Uni- and multi-variate Cox proportional hazard and linear/logistics regression models were used to stratify and evaluate individual factor's contribution. The clinical significance of the results is taken as p value of <0.05, corresponding to $>95\%$ confidence interval.

3. Results

The patient profile and disease characteristics are summarized in Table 1. A total of 206 patients were recruited, with the median age of 68.5 years old (range: 48.0–85.0 years). Median prostate volume was 31.0 mL (range 10.0–97.0 mL). Transrectal ultrasound biopsy was the most common method of diagnosis. Risk stratification was based on the D'Amico classification: 25 patients (12.1%) low risk, 69 (33.5%) intermediate risk, and 112 (54.4%) high risk.

All patients received IMRT ranging from 70 to 74 Gy. One hundred and eight-five patients (89.8%) received concomitant hormonal therapy. The median time to PSA nadir was 7 months and the median PSA nadir value was 0.03 ng/mL, partly due to the significant proportion of patients who had adjuvant hormonal therapy in our study group.

Sixty-one patients (29.6%) experienced the PSA bounce phenomenon, at a median time of 16 months (range 6–36 months), with a median magnitude of 0.35 ng/mL (range 0.1–4.2 ng/mL) and for a median duration of 12 months (range 5–38 months) (Table 2). Age was a significant consistent predictor of PSA bounce. When stratified, younger patients (aged <65 years) were associated with 3 times higher likelihood to experience bounce ($p = 0.001$), for a longer duration ($p = 0.022$) and with greater magnitude, although not statistically significant ($p = 0.113$).

Table 1 Patient demographics.

Parameter	Value
Age (year), median (range)	68.5 (48.0–85.0)
Risk stratification, *n* (%) [D' Amico Classification]	
Low	25 (12.1)
Intermediate	69 (33.5)
High	112 (54.4)
Prostate volume (mL), median (range)	31.0 (10.0–97.0)
Adjuvant hormonal therapy, *n* (%)	
Yes	185 (89.8)
No	21 (10.2)