Original Article

Correlation Between Serum Prostate-Specific Antigen and Testosterone Following Bilateral Total Orchidectomy for Patients with Advanced Prostate Cancer in Jos, Nigeria

Abstract

Background: Prostate cancer is a common malignancy affecting men beyond the middle age. Monitoring of treatment of the disease using serum testosterone and prostate-specific antigen (PSA) offers an index of treatment efficacy and a reflection of disease progression, respectively. The objective of this study was to determine the relationship between changing values of serum PSA and serum testosterone in patients with advanced prostate cancer following bilateral total orchidectomy (BTO). **Materials and Methods:** This was a prospective longitudinal study carried out over a 1-year period among patients who met the inclusion criteria. Each patient underwent detailed clinical evaluation including history, as well as physical examination with digital rectal examination of the prostate. Also, samples of serum PSA and testosterone were obtained and sent to the same chemical pathology laboratory before intervention with BTO, then at 2, 4, and 6 months. The values of serum PSA and testosterone were obtained and changes over this period were compared for both parameters. The analyses included independent inferential analysis of serum testosterone and serum PSA over a period of 6 months and a correlation of the two parameters over the same period. Results were analysed using SPSS version 23. *P* value of <0.05 was regarded significant. Charts and tables were used for data expression. Kruskal–Wallis and Wilcoxon tests were used for individual inferential analysis of serum testosterone and PSA. The Spearman ranked correlation coefficient test was used to determine the degree of correlation of serum testosterone and serum PSA levels while Pearson correlation coefficient test was used to determine the degree of correlation between the percentage changes in serum testosterone and PSA measured over the period of the study. **Results:** A total of forty-two men with mean age of 68.49 ± 8.86 years who had advanced prostate cancer were recruited. The histologic type of prostate cancer diagnosed for all the patients was adenocarcinoma. The mean Gleason score was 7.98 ± 1.09, while the modal Gleason grade group represented was grade group 5. There were statistically significant changes in serum testosterone and PSA levels in response to bilateral total orchidectomy with *P* value of <0.001. However, there was no statistically significant correlation between serum testosterone and serum PSA levels following bilateral total orchidectomy with p values of 0.492, 0.358, 0.134, and 0.842 at baseline, 2, 4, and 6 months, respectively. There was a significant correlation between the percentage changes in serum testosterone and PSA measured between baseline and 2 months with *P* value of <0.001. However, there was no statistically significant correlation between the percentage changes in serum testosterone and PSA measured between baseline measured against 4 months and 6 months with *P* value of 0.998 and 0.638, respectively. **Conclusion:** The study showed that reduction in serum levels of testosterone and PSA following BTO was significant. It also revealed no statistically significant correlation between serum testosterone and serum PSA measured over 6 months following bilateral total orchidectomy.

Keywords: *Advanced prostate cancer, BTO, PSA, testosterone*

Olutayo Israel Osunaiye[1], Venyil Mamzhi Ramyil[2], Nuhu Kutan Dakum[2], Idorenyin Cletus Akpayak[2], Samaila Ibrahim Shuaibu[2], Chimaobi Gideon Ofoha[2], Ayodeji Olushola Ogunmola[1], Christian Agbo Agbo, Adedayo Stephen Oyedeji,

Urology Division, Department of Surgery, Jos University Teaching Hospital, Jos, [1]Urology Division, Department of Surgery, Federal Medical Centre, Lokoja, [2]Department of Surgery, College of Medical Sciences, University of Jos, Jos, Nigeria

Received: 01-Nov-2022
Accepted: 09-Dec-2022
Published: 20-Mar-2023

Address for correspondence:
Dr. Olutayo Israel Osunaiye, Department Of Surgery, Federal Medical Centre, P.M.B 1001, No.1 Salihu Ibrahim Road, Lokoja, Kogi State, Nigeria. E-mail: olutayoosunaiye@gmail.com

Access this article online

Website: www.jwacs-jcoac.com

DOI: 10.4103/jwas.jwas_274_22

Quick Response Code:

Introduction

Prostate cancer is one of the most common malignancies afflicting men worldwide.[1,2] The incidence is highest among African-Americans with that of Nigeria reported by Osegbe *et al.*[3] to be 127 per 100,000 cases.

Locally advanced prostate cancer is defined as tumour that has extended clinically beyond the prostatic capsule (clinical stage T3a), with invasion of the pericapsular tissue, prostatic apex, seminal vesicles (T3c) and bladder neck (T4a), with regional lymph node involvement but no distant metastasis (T3-4N ± M0).[4]

How to cite this article: Osunaiye OI, Ramyil VM, Dakum NK, Akpayak IC, Shuaibu SI, Ofoha CG, *et al.* Correlation between serum prostate-specific antigen and testosterone following bilateral total orchidectomy for patients with advanced prostate cancer in Jos, Nigeria. J West Afr Coll Surg 2023;13:82-91.

Advanced prostate cancer however includes any combination of lymphatic, blood, or contiguous local spread. Manifestations of this may include anaemia, bone marrow suppression, pathological fractures, spinal cord compression, haematuria, bladder outlet obstruction, chronic renal failure, and symptoms related to metastases.[5]

Prostate-specific antigen (PSA) is a glycoprotein produced mainly by the epithelial cells of the prostate and released mainly into semen and blood.[2] The primary release of PSA into the seminal fluid results in 10^6 fold higher seminal concentrations than levels measured within the serum.[6] The levels of serum PSA rise mainly in prostate cancer, benign prostatic hyperplasia (BPH) and prostatitis. PSA testing is therefore widely used in screening for prostate cancer, monitoring disease progression and response to treatment.[7]

Prostate cancer is a malignancy of the prostate gland, an androgen target organ. It is therefore predominantly hormone sensitive at the early stage of its natural history.[8] Testosterone, which is the major male sex hormone to which prostatic tissue and cancer cells respond, contribute up to 90% of circulating androgenic activity which is needed for normal reproductive and sexual function.[9,10] About 90% of it is produced by the Leydig cells of the testes which in turn is regulated by the pituitary gland and the hypothalamus. Testosterone, itself, acts on the epithelial cells of the prostate to stimulate PSA production.[11,12]

Testosterone levels may have a major influence on PSA values in patients with prostate cancer. The postulated mechanism consists of free testosterone taken up by the prostatic epithelial cells, converted to 5 alpha dihydrotestosterone by 5 alpha reductase type II, bound to the androgen receptor and afterwards interacting with the androgen response element located upstream from the PSA gene.[13]

Androgen withdrawal causes a retardation of prostate cells and tumour growth, thought to be from programmed cell death and ischaemic injury from anoxia.[14] This, expectedly also leads to depletion of serum PSA. Thus, manipulation of the hormonal milieu and depletion of testosterone reserves play a role in the treatment of prostate cancer and often decreases morbidity and increases survival. This is the concept of androgen deprivation therapy (ADT).[15-17]

The measure of testosterone value in a patient with advanced prostate cancer could give an index of response to treatment, progression, or remission of the disease.

Prostate cancer constitutes such a disease burden that within the last two decades has become the most common non-cutaneous malignancy in males with its incidence haven risen 3.7 fold over this period.[1,18] It has also become the second leading cause of cancer deaths after lung cancer in men in the United States over the last decade.[19]

The aim of the study is to determine the relationship between changing values of serum PSA and serum testosterone following bilateral total orchidectomy (BTO) in patients with advanced prostate cancer.

Patients and Methods

This was a hospital based prospective longitudinal study carried out at Jos University Teaching Hospital (JUTH) between 1st February 2019 and 31st January 2020. Patients with advanced prostate cancer who opted for surgical androgen deprivation therapy were recruited for the study. Patients already commenced on medical androgen deprivation therapy and those who had sub-optimal baseline testosterone were excluded from the study.

Consent for the study was obtained from the Research and Ethics Committee of JUTH. Informed consent was obtained from patients who fulfilled the criteria for inclusion in the study and agreed to participate in the study.

A total of forty-two patients were recruited consecutively for the study. All the patients were issued a study identification number (SIN) based on their sequence of enrolment into the study and underwent clinical evaluation including digital rectal examination. Also, samples of serum PSA and testosterone were obtained and sent to the same chemical pathology laboratory and analysed uniformly by the same chemical pathologist using corresponding reagents (chemiluminescence immunoassay for PSA and enzyme linked immunosorbent assay for testosterone) before intervention with BTO, then at 2, 4, and 6 months. The values of serum PSA and testosterone were obtained and changes over this period were compared for both parameters.

Data were obtained using a structured proforma which included the patients' bio-demographics, clinical details such as DRE findings, metastatic features (where present), histology details with Gleason score, grade and grade group, abdominopelvic ultrasound findings, serum testosterone, and serum total PSA values (Appendix II). Due to the absence of the ideal tumour staging modality at the study centre, patients with the advanced stage of the disease were identified through DRE findings and clinical history supported by radiologic investigations such as skeletal X-rays and abdomino-pelvic ultrasonography.

Results were analysed using Statistical Package for Social Services (SPSS) version 23. Charts and tables were used to express the data. Kruskal–Wallis and Wilcoxon tests were used for independent inferential analysis of serum testosterone and PSA respectively. The Spearman's rank correlation test was used to determine the degree of correlation of the changing values of serum testosterone and serum PSA over 6 months while Pearson correlation coefficient test was used to determine the degree of correlation between the percentage changes in serum

testosterone and PSA measured over the period of the study. A P value < 0.05 was considered significant for inferential statistical analysis.

The limitation of the study was that the standard to investigative modality for prostate cancer staging, namely, multi-parametric magnetic resonance imaging was not available at the institution where the study was carried out.

Results

A total of forty-two patients who met the inclusion criteria and gave consent were recruited for the study with each followed up for 6 months. The age range of the subjects was from 53 to 87 years with mean age of 68.49 ± 8.86 years and age distribution given in Table 1.

Digital rectal examination (DRE) of 36 out the 42 subjects (86%) revealed one or more of findings suggestive of prostate malignancy. Trans-abdominal ultrasound estimation of prostate volume revealed values which ranged from 30 to 649 ml with a median value of prostate volume of 77.5 ml (IQR: 55.75–126.78).

The histologic type of prostate cancer diagnosed for all the patients recruited was adenocarcinoma with the Gleason scores ranging between 6 and 10. The mean Gleason score was 7.98 ± 1.09. The modal Gleason grade group represented was grade group 5 [Figure 1].

The changes in median values of serum testosterone measured across the period of the study are represented by a Kruskal–Wallis test value of 129.17 with a P value of <0.001 [Table 2]. Using the same test, a value of 93.42 represents the changes in median values of serum PSA values measured across the period of the study with P value of <0.001 [Table 3].

Table 1: Age distribution of 42 subjects with advanced prostate cancer

Age group	Frequency	Percentages
50–59	7	16.7
60–69	16	38.1
70–79	14	33.3
80–89	5	11.9
Total	42	100

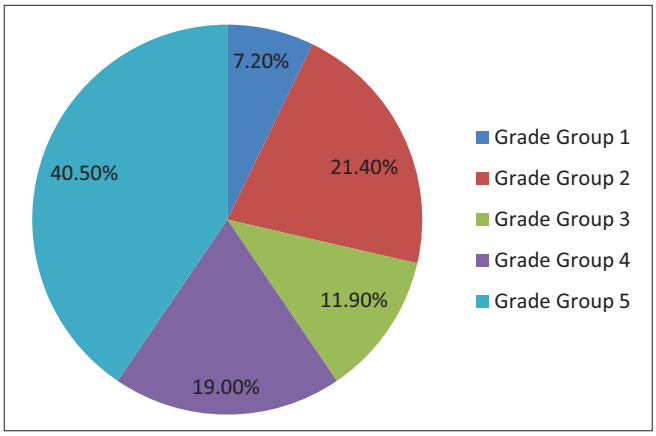

Figure 1: Gleason grade group distribution of 42 subjects

The changes obtained in median serum testosterone values at 2, 4, and 6 months post bilateral total orchidectomy (BTO) from median baseline value were represented by Wilcoxon test values of 903.0, 902.0 and 902.0, respectively, and with P values of <0.001 across board. Using the same test, the changes in median serum PSA values obtained at 2, 4, and 6 months post BTO were represented by values of 974.0, 934.0, and 919.0 with universal P values of <0.001.

The mean percentage reduction in serum testosterone obtained at 2, 4, and 6 months post BTO from the baseline were –95.52%, –98.01%, and –98.99%, respectively, with each percentage reduction within its corresponding confidence interval as shown in Table 4. The mean percentage reduction in serum PSA from baseline to 2, 4, and 6 months post BTO were –92.65%, –96.12%, and –97.48%, respectively, with each percentage reduction within its corresponding confidence interval [Table 5].

The correlation between serum testosterone and PSA levels at baseline, 2 months, 4 months, and 6 months post BTO were represented by Spearman ranked correlation coefficient (r value) of 0.110, 0.146, 0.235, and –0.320 with P value of 0.492, 0.358, 0.134, and 0.842 respectively [Figures 2–5].

The correlation between the mean percentage changes in serum testosterone and PSA with the value at the baseline measured against the values obtained at 2 months, 4 months, 6 six months is represented by Pearson correlation coefficient (r value) of 0.515, 0.001, and –0.075 with P values of <0.001, 0.998, and 0.638, respectively [Table 6].

Discussion

This study measured the response of serum testosterone and serum PSA to bilateral total orchidectomy and also determined the relationship between changing values of serum testosterone and serum PSA following bilateral total orchidectomy.

In this study, 42 patients with histologic diagnosis of prostate cancer in the advanced stage were recruited and studied. Most of the patients presented in the seventh decade of life with mean age of 68.49 ± 8.86 years. This is similar to reports from other studies which identified the seventh decade of life as the mean age of diagnosis. Osegbe *et al*.[3] and Udeh *et al*.[20] reported 68.3 and 65.57 as the respective mean ages for prostate cancer diagnosis in Nigeria. Similarly, Ezenwa *et al*.[21] reported the 7th decade of life as the decade for peak incidence of prostate cancer in Nigeria.

Table 2: Changes in testosterone following BTO in patients with prostate cancer

Parameters	Period	Median (IQR)	Kruskal–Wallis	*P* value
Testosterone	Baseline	437.75 (370.88–634.25)	129.97	<0.001
	2 months	17.53 (5.08–12.30)		
	4 months	7.92 (5.08–12.30)		
	6 months	3.45 (1.67–6.64)		

BTO: bilateral total orchidectomy, IQR: interquartile range

Table 3: Changes in PSA level following BTO in patients with advanced prostate cancer

Parameter	Period	Median (IQR)	Kruskal–Wallis	*P* value
PSA (ng/ml)	Baseline	147.96 (89.45–1012.25)	93.42	<0.001
	2 months	8.29 (3.19–48.69)		
	4 months	4.38 (1.52–25.49)		
	6 months	2.22 (0.65–13.29)		

BTO: bilateral total orchidectomy, IQR: interquartile range, PSA: prostate-specific antigen

Table 4: Mean percentage reduction in testosterone at different periods from baseline

Parameter	Periods compared	Mean percentage reduction	95% confidence interval
Testosterone	Baseline/2 months	–95.52	–96.52 to –94.52
	Baseline/4 months	–98.01	–98.38 to –97.64
	Baseline/6 months	–98.99	–99.26 to –98.71

Table 5: Mean percentage reduction in PSA levels at different periods from the baseline

Parameter	Periods compared	Mean percentage reduction	95% confidence interval
PSA	Baseline/2 months	–92.65	–96.51 to –88.80
	Baseline/4 months	–96.12	–98.72 to –93.51
	Baseline/6 months	–97.48	–99.61 to –95.34

PSA: prostate-specific antigen

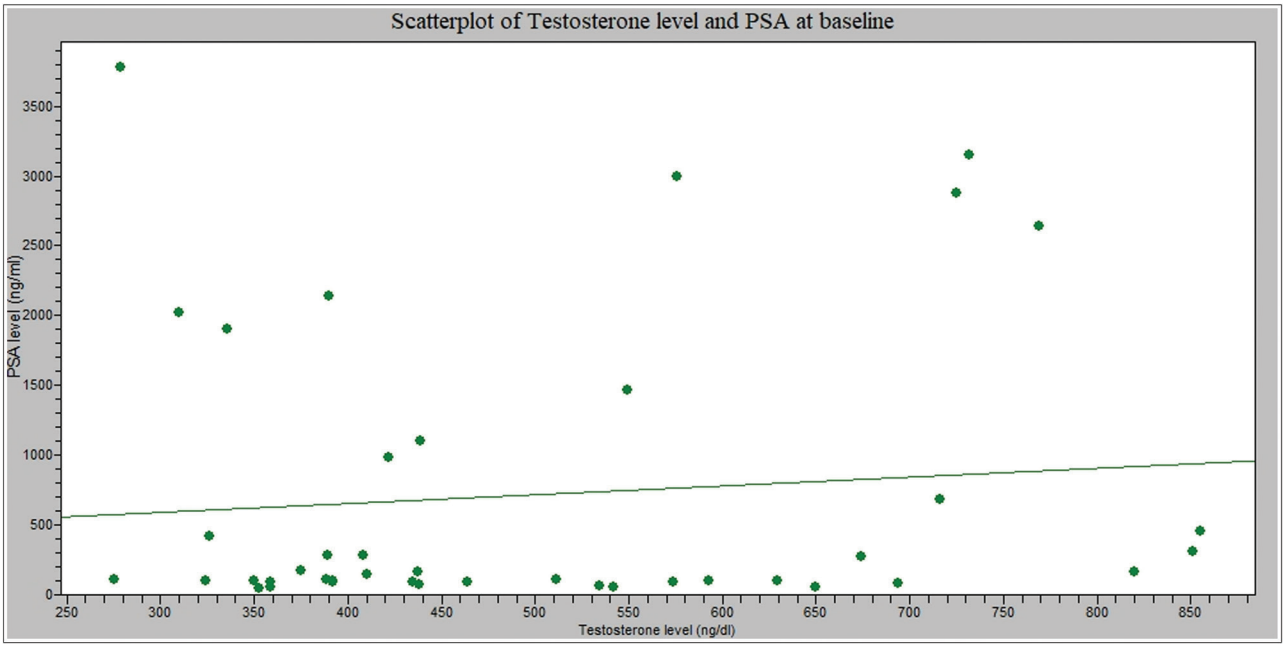

Figure 2: Degree of correlation between testosterone and PSA levels at the base-line (*P* value: 0.492, Spearman ranked correlation coefficient (*r*): 0.11)

This study demonstrated that the level to which serum testosterone dropped from the pre-operative value to those obtained over the periods considered after bilateral total orchidectomy (2 months, 4 months, and 6 months) was statistically significant (p was <0.001 where significant P value is <0.05). Smith[22] conducted a study among 49 men

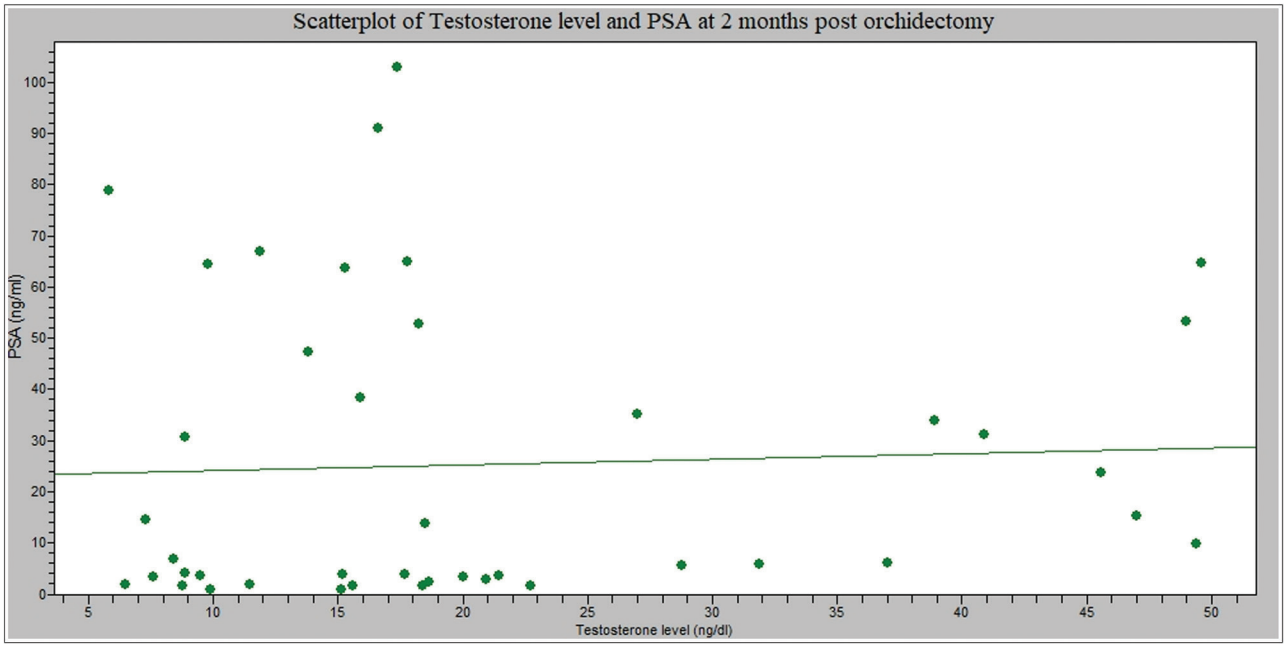

Figure 3: Degree of correlation between testosterone and PSA levels at 2 months (*P* value: 0.358, *r*: 0.146)

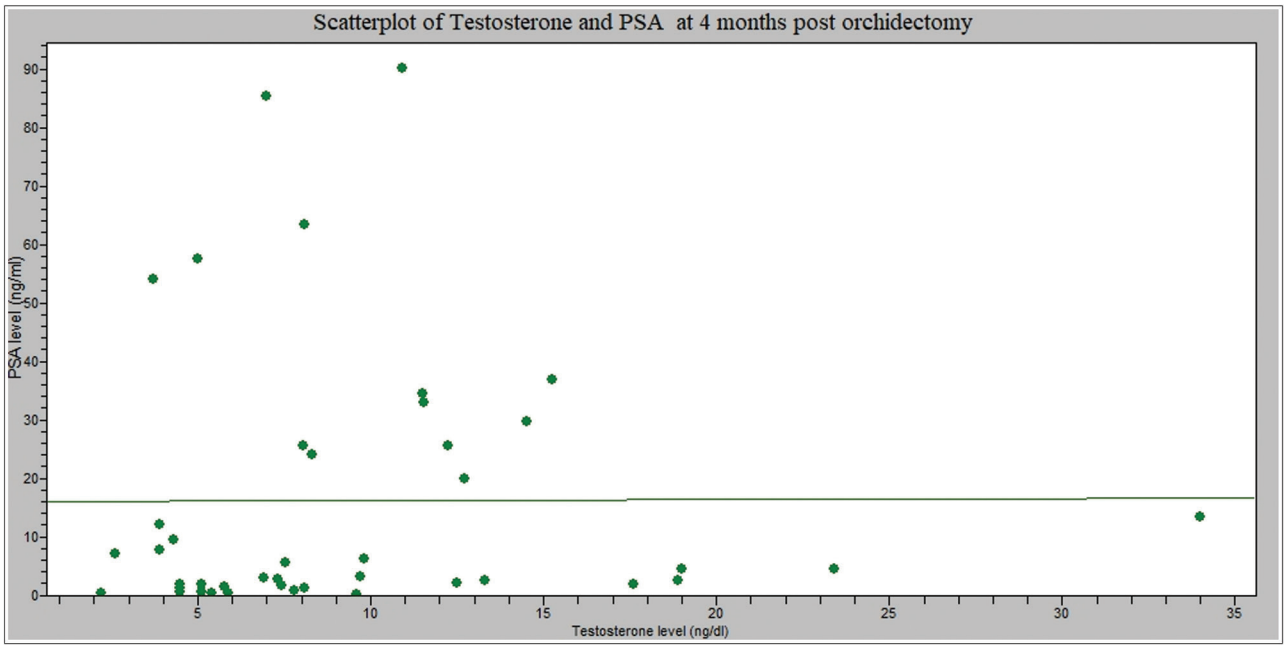

Figure 4: Degree of correlation between testosterone and PSA levels at 4 months (*P* value: 0.134, *r*: 0.235)

with locally advanced/recurrent prostate cancer in which serum testosterone was measured at baseline, 24 weeks and 48 weeks during ADT with Leuprolide injection given 3 monthly for 48 weeks and found statistically significant reduction in value. Rohi *et al.*[23] conducted a study among 40 male patients treated with bilateral orchidectomy for advanced prostate cancer which yielded similar results. All the values at the various stages of follow-up depicted statistically significant reduction from baseline as they fell within their corresponding confidence intervals. This indicates that within similar circumstances as seen in both studies, serum testosterone can be expected to reduce significantly in response to bilateral total orchidectomy.

The changes in the post-operative levels of serum PSA measured in this study at 2 months, 4 months, and 6 months post BTO were statistically significant when compared to the baseline. A study was carried out by Atta *et al.*[24] which involved 33 men with metastatic prostate cancer measured serum PSA changes over a period of 6 months following BTO. It revealed a reduction in mean serum PSA from a pre orchidectomy value of 240.89 ng/ml to a 6-month post orchidectomy value of 9.37 ng/ml. It was however not

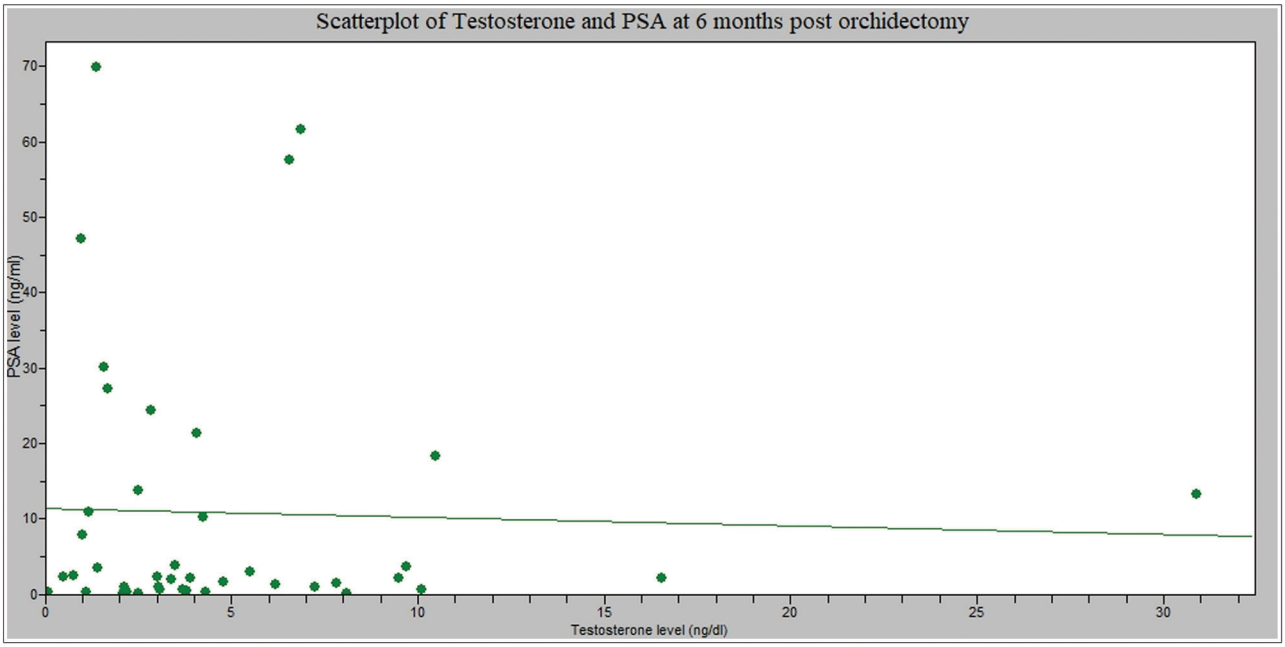

Figure 5: Degree of correlation between testosterone and PSA levels at 6 months (*P* value: 0.842, *r*: –0.32)

Table 6: Correlation between percentage changes in serum testosterone and PSA at different periods of follow-up measured against the baseline

Parameters testosterone (ng/dl)/PSA (ng/ml)	Study period	Pearson correlation coefficient	Strength of association (r^2)	*P* value
	Baseline/2 months	0.515	0.27	< 0.001
	Baseline/4 months	0.001	0.00	0.998
	Baseline/6 months	–0.075	0.01	0.638

PSA: prostate-specific antigen

determined if the reduction in serum PSA noticed over the follow-up period was statistically significant.

This study also revealed a mean percentage reduction in serum testosterone of –98.99% at 6 months post BTO when measured against the baseline value. This is statistically significant and falls within the confidence interval (CI) of –99.26% to –98.71%. Attar Shakir,[25] in an earlier study reported a mean percentage reduction in serum testosterone of –64% after surgery in a study involving a subset of men at 2 years post BTO for metastatic prostate cancer. There was a measurable percentage reduction in serum testosterone in these studies. However, it cannot be determined whether they are statistically significant as the confidence intervals were not stated. Measurement of the mean percentage change of testosterone at a different time of follow-up for the above studies compared to the index study might have accounted for the different percentage change observed. This finding suggests that timing of follow-up monitoring affects the degree of accuracy, uniformity, and reproducibility of follow-up parameters.

In this study, there was also a significant mean percentage reduction in serum PSA over 6 months when measured against the baseline. The study revealed a –97.48% (CI: –99.61 to –95.34) reduction in serum PSA level at 6 months when measured against the baseline PSA level. A similar result was reported by Atta *et al.*[24] who found a percentage reduction in serum PSA of –91.9% 6 months after BTO in a study involving thirty-three patients with metastatic prostate cancer. The study was carried out in a smaller subset of subjects which might have affected the degree of statistical accuracy, hence the difference in percentage change when compared with the index study.

This study showed no statistically significant correlation between serum testosterone levels and serum PSA levels following bilateral total orchidectomy with *P* values of 0.492, 0.358, 0.134 and 0.842 at baseline (pre-orchidectomy) and at 2, 4, and 6 months post orchidectomy, respectively. A study carried out by Reis *et al.*[26] to assess testosterone and PSA kinetics among patients with advanced prostate cancer using diverse chemical castration techniques found no linear correlation between serum testosterone and PSA after 3 months of ADT using the Spearman correlation coefficient. Another study by Chen *et al.*[27] measured the correlation between serum hormone levels and treatment outcome parameters including PSA among patients

with metastatic prostate cancer. A subset consisting of 77 patients treated with orchidectomy had a mean pre-treatment testosterone and PSA of 4 ng/ml and 143.1 ng/ml, respectively. These all went on to have castrate level of testosterone (study reference value of <0.2 ng/ml) and PSA nadir of <4 ng/ml. The study reported no statistically significant correlation.

Conversely, a study carried out by Perachino *et al.*[28] among 129 consecutive patients with metastatic prostate cancer who had androgen deprivation found a direct relationship between the monitored values of serum testosterone and serum PSA over 6 months with the later measured as part of the parameters that formed the predictors of survival of the subjects. This was however, a retrospective study which involved a much longer duration and also utilised a multivariate statistical model for data analysis. These, in addition to the medical method of androgen deprivation utilised might have had contributory roles in furnishing a different outcome as compared with the index study.

Finally, this study revealed a significant correlation between the percentage changes in serum testosterone and PSA measured between baseline and 2 months with *P* value of <0.001.

It however showed no statistically significant correlation between the percentage changes in serum testosterone and PSA measured between baseline against 4 months and 6 months with *P* value of 0.998 and 0.638, respectively. The alteration of the pattern of linear relationship of the percentage changes between both parameters over the period of follow-up might suggest possible subclinical tumour progression while disease is yet in the castrate state. No study was identified which measured the correlation between the percentage changes in serum testosterone and PSA following bilateral total orchidectomy.

Conclusion

This study showed that there was statistically significant reduction in both serum testosterone and PSA levels when measured independently in response to bilateral total orchidectomy.

There was however no statistically significant correlation between serum testosterone and serum PSA levels following bilateral total orchidectomy at baseline, 2, 4, and 6 months. Also, there was essentially no statistically significant correlation between the percentage changes in serum testosterone and PSA over the period of the study.

Recommendation

The overall findings of non-correlation of changes in both the standard unit values and percentages of both serum testosterone and PSA during the period of monitoring suggest that correlated values of serum testosterone and PSA may not offer any significant benefit or added role in the monitoring of patients on ADT. As such, further studies along this domain may not be of any particular benefit.

Acknowledgements

I wish to appreciate the Almighty God and acknowledge Prof. B.T Ugwu and Dr. T.O Afolaranmi for professional advice/logistics and statistical analysis respectively. Also, all team members are appreciated. May God continue to bless you all.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Stephenson AJ, Klein EA. Epidermiology, etiology, and prevention of prostate cancer. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016. p. 2543-64.
2. Yeboah E, Olopade-Olaopa E, Kyei M. The prostate gland. In: Archampong E , Naaeder S, Ugwu B, editors. Baja's Principles and Practice of Surgery Including Pathology in the Tropics. 5th ed. Tema: Ghana Publishing Corporation; 2015. p. 967-1002.
3. Osegbe DN. Prostate cancer in Nigerians: Facts and nonfacts. J Urol 1997;157:1340-3.
4. Meng VM, Carroll PR. Treatment of locally advanced prostate cancer. In: Wein AJ, Partin AW, Kavoussi LR, Peters CA, editors. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016. p. 2752-68.
5. Martha KT, Shaukat MQ. Metastatic and advanced prostate [Internet]. Medscape. 2017 [cited 21 Feb 2018]. Available from: https://emedicine.medscape.com/article/454114-overview. [Last accessed on 14 April 2018].
6. Todd M, Ganesh S, Alan W. Prostate cancer tumour marker. In: Wein AJ, Partin AW, Kavoussi LR, Peter CA, editors. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016. p. 2565-77.
7. Velonas VM, Woo HH, dos Remedios CG, Assinder SJ. Current status of biomarkers for prostate cancer. Int J Mol Sci 2013;14:11034-60.
8. Nelson PS, Clegg N, Arnold H, Ferguson C, Bonham M, White J, *et al*. The program of androgen-responsive genes in neoplastic prostate epithelium. Proc Natl Acad Sci U S A 2002;99:11890-5.
9. Buttyan R, Ghafar MA, Shabsigh A. The effects of androgen deprivation on the prostate gland: Cell death mediated by vascular regression. Curr Opin Urol 2000;10:415-20.
10. Sharifi N, Gulley JL, Dahut WL. Androgen deprivation therapy for prostate cancer. JAMA 2005;294:238-44.
11. Gomella LG, Singh J, Lallas C, Trabulsi EJ. Hormone therapy in the management of prostate cancer: Evidence-based approaches. Ther Adv Urol 2010;2:171-81.
12. Turek PJ. Male reproductive physiology. In: Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016. p. 516-37.
13. Kokontis J, Takakura K, Hay N, Liao S. Increased androgen receptor activity and altered c-myc expression in prostate cancer cells after long-term androgen deprivation. Cancer Res 1994;54:1566-73.
14. Huggins C, Stevens RE Jr, Hodges CV. Studies on prostatic

cancer: II. The effects of castration on advanced carcinoma of the prostate gland. Arch Surg 1941;43:209-23.
15. Bolla M, Gonzalez D, Warde P, Dubois JB, Mirimanoff RO, Storme G, *et al*. Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin. N Engl J Med 1997;337:295-300.
16. MRC. The Medical Research Council Prostate Cancer Working Party Investigators Group. Immediate versus deferred treatment for advanced prostatic cancer: Initial results of the Medical Research Council Trial. Br J Urol 1997;79:235-46.
17. Nelson JB. Hormonal therapy for prostate cancer. In: Wein AJ, Partin AW, Kavoussi LR, editors. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016. p. 2786-803.
18. Pishgar F, Ebrahimi H, Moghaddam SS, Fitzmaurice C. Global, regional and national burden of prostate cancer, 1990 to 2005: Results from the global burden of disease study 2015. J Urol 2018;199:1232.
19. Moul JW. The evolving definition of advanced prostate cancer. Rev Urol 2004;6:10-17.
20. Udeh EI, Nnabugwu II, Ozoemena FO, Ugwumba FO, Aderibigbe AS, Ohayi SR, *et al*. Prostate-specific antigen density values among patients with symptomatic prostatic enlargement in Nigeria. World J Surg Oncol 2016;14:174.
21. Ezenwa E, Tijani K, Jeje A, Ogunjimi A, Ojewola R. Prevalence of prostate cancer among Nigerians with intermediate total prostate specific antigen levels (4–10 ng/ml): Experience at Lagos University Teaching Hospital, Nigeria. Int J Urol 2012;9:1-5.
22. Smith MR. Obesity and sex steroids during gonadotropin-releasing hormone agonist treatment for prostate cancer. Clin Cancer Res 2007;13:241-5.
23. Røhl HF, Beuke HP. Effect of orchidectomy on serum concentrations of testosterone and dihydrotestosterone in patients with prostatic cancer. Scand J Urol Nephrol 1992;26: 11-4.
24. Atta MA, Elabbady A, Sameh W, Sharafeldeen M, Elsaqa M. Is there still a role for bilateral orchidectomy in androgen-deprivation therapy for metastatic prostate cancer? Arab J Urol 2020;18:9-13.
25. Shakir Attar F. Comparative study between orchidectomy alone and orchidectomy with hormonal therapy (combined androgen blockade) for patients with advanced carcinoma of the prostate. Basrah J Surg 2010;16:95-101.
26. Reis LO, Denardi F, Faria EF, Silva ED. Correlation between testosterone and Psa kinetics in metastatic prostate cancer patients treated with diverse chemical castrations. Am J Mens Health 2015;9:430-4.
27. Chen SS, Chen KK, Lin AT, Chang YH, Wu HH, Chang LS. The correlation between pretreatment serum hormone levels and treatment outcome for patients with prostatic cancer and bony metastasis. Bju Int 2002;89:710-3.
28. Perachino M, Cavalli V, Bravi F. Testosterone levels in patients with metastatic prostate cancer treated with luteinizing hormone-releasing hormone therapy: Prognostic significance? Bju Int 2010;105:648-51.