

# Correlation of Detrusor Wall Thickness with International Prostate Symptom Score: A Cross-sectional Study of Nigerian Men with Prostate-Related Diseases

OBASI AUGUSTINE ULEBE<sup>1</sup>, TIMOTHY UZOMA MBAERI<sup>2</sup>, JOSEPH AMAUZO ABIAHU<sup>3</sup>, MICHAEL ECHETA ARONU<sup>4</sup>, KINGSLEY CHIDI ORANUSI<sup>5</sup>, ALEXANDER MADUABUROCHUKWU NWOFOR<sup>6</sup>, JIDEFOR CHUKWUMA ORAKWE<sup>7</sup>, OKECHUKWU OBIORA MBONU<sup>8</sup>



## ABSTRACT

**Introduction:** Bladder Outlet Obstruction (BOO) due to prostate-related diseases can lead to changes in bladder wall resulting in detrusor wall thickening. These changes are time-dependent and may reflect the severity of underlying BOO. Although urodynamic tests are considered to be the gold standard for the assessment of the severity of Lower Urinary Tract Symptoms (LUTS), these are time-consuming, invasive and expensive. The Detrusor Wall Thickness (DWT) measurement has emerged as a cheap, non invasive and reproducible alternative means of assessing the severity of LUTS in men with BOO.

**Aim:** To determine the correlation between the DWT and International Prostate Symptom Score (IPSS) in men being evaluated for prostate-related BOO/LUTS.

**Materials and Methods:** A cross-sectional hospital based study was conducted over a period of 12 months (May 2014 to April 2015), at Urology Clinics of the Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi. All 100 new consecutive male patients aged  $\geq 40$  years with prostate-related LUTS and who can achieve bladder volume of  $>250$  mL were included in the study. The DWT

was measured at three different sites (anterior, lateral and dome) at bladder volume  $>250$  mL. Ethical approval was attained from the institutional ethical review board. Severity of LUTS was assessed using a validated IPSS questionnaire. Data was analysed using SPSS version 20. Spearman's correlation was used to assess the correlation. The p-value  $<0.05$  was considered significant.

**Results:** A total of 100 men with the mean age of  $71.02 \pm 9.10$  years were studied. The mean duration of symptoms was  $30.63 \pm 26.60$  months with the average IPSS being  $20.94 \pm 6.13$ . A total of 43 patients and 57 patients had moderate and severe LUTS, respectively. None of the patients had mild LUTS. The mean anterior, lateral, dome and average DWT measurements were  $4.95 \pm 2.36$  mm,  $4.96 \pm 2.37$  mm,  $5.02 \pm 2.34$  mm and  $4.97 \pm 2.35$  mm, respectively. A total of 97 patients had DWT  $\geq 2$  mm. There was a significant positive correlation between the DWT and IPSS ( $r^2=0.635$  and  $p<0.001$ ).

**Conclusion:** The positive correlation between the DWT and IPSS has demonstrated that the DWT measurement can be used in assessing the severity of LUTS in men with prostate-related diseases.

**Keywords:** Benign prostatic hyperplasia, Bladder outlet obstruction, Ultrasound

## INTRODUCTION

The BOO is a common problem in older men and is often associated with prostate-related diseases and LUTS [1]. This BOO is found urodynamically in 60% of symptomatic patients with Benign Prostate Hyperplasia (BPH), and in 52% of asymptomatic patients [2,3]. The BOO causes changes in bladder wall and function leading to detrusor wall thickening and other ultra-structural changes [4-6]. These changes in bladder wall are time-dependent and may reflect the severity of the underlying BOO [7-9]. In 2002, Tubaro A and Miano L explained that the thickening of the detrusor muscle resulted from increased work load, similar to the heart muscle hypertrophy seen in a valvular stenosis or systemic arterial hypertension [10]. From this analogy, it was hypothesised that the thickening of the detrusor wall reflects the increased work load of the bladder and provides information about the degree of BOO [10].

Although, urodynamic tests are considered as the gold standard for the diagnosis of BOO, they are invasive, time-consuming and expensive [11]. Ultrasound DWT measurements have the advantages of being non invasive, inexpensive, quick, easily accessible, reproducible with high diagnostic accuracy and does not involve the use of contrast materials/ionising radiation [12,13].

The severity of LUTS can be assessed using the IPSS which is a modification of American Urological Association (AUA) symptom

score with an inclusion of Quality of Life (QoL) assessment index [14,15]. Patients were categorised according to the severity of LUTS into mild (score 0-7), moderate (score 8-19) and severe (score 20-35). The ultrasound DWT measurement is an ideal method that significantly correlates with the severity of LUTS as assessed with IPSS in men with prostate-related diseases [16-18]. Hence, the DWT can serve as a potent predictor of the severity of LUTS which also correlates with Pressure Flow Studies (PFS) and may replace PFS in the near future as non invasive alternative assessment tool [19].

Considering the high specificity and sensitivity of the DWT measurement, it may serve as a veritable tool in assessment, treatment and follow-up of men with prostate-related BOO/LUTS [16,17,20]. However, there is need to standardise and streamline the measurement techniques in order to enhance reproducibility and repeatability of results.

Most of the studies [16-18,21,22] on the DWT were conducted in western countries among Caucasians with few done among the blacks especially in Nigeria [23,24]. However, none of these local studies on DWT measurements to the best of our knowledge have studied the relationship between the DWT and IPSS amongst patients with prostate-related LUTS. Due to paucity of similar local studies, it was deemed necessary to conduct this research.

The aim of the study was to determine the correlation between the DWT and IPSS among adult Nigerian male patients with prostate-related BOO/LUTS.

## MATERIALS AND METHODS

A cross-sectional hospital based study was conducted amongst 100 new consecutive adult male patients with prostate related (BPH, Prostate cancer and Chronic Prostatitis) LUTS who presented to Urology Clinics of NAUTH. This is a tertiary healthcare facility located in the commercial city of Nnewi in Anambra State, Southeast, Nigeria. This hospital serves as major referral center in the region. The study was conducted from May 2014 to April 2015.

Ethical approval was obtained from the institutional ethical review board and written informed consent was obtained from all the participants (IRC/IERB number: NAUTH/CS/66/VOL5/63).

The sample size was calculated using Leslie Fischer's statistical formula [25] as shown below:

$$nf = \frac{n}{1+n/N}$$

Where, nf=the desired sample size (if target population is less than 10,000).

n=the desired sample size when population is more than 10,000.

From NAUTH Surgical Out Patient (SOP) clinics Registry, an average of three patients with prostate-related LUTS were examined per week. Therefore, an average total of 156 patients will be expected to be examined in 52 weeks. Therefore, N=156

But from Cochran formula [26]:

$$n = \frac{Z^2 pq}{d^2}$$

Where:

p=Prevalence rate=25% (25% prevalence rate of prostate-related LUTS as documented in the study by Ezeanyika LUS et al., [27] was used).

q=The remaining proportion not likely to have prostate-related LUTS. But q=1-p, hence q=75%.

d= the level of statistical significance which is taken as 5% (0.05) for this study.

Z=the standard normal deviation at required confidence level of 1.96.

Therefore,

$$n = \frac{(1.96)^2(0.25)(0.75)}{(0.05)^2}$$

=approximately 288.12

Thus, nf=288.12/(1+288.12/156)

=99.93.

Therefore, approximately 100 patients were recruited into this study.

Purposive total sampling technique was used in recruiting the patients within the study period.

**Inclusion criteria:** All new consecutive male patients aged  $\geq 40$  years with prostate-related LUTS who voluntarily gave their consent and who were capable of achieving bladder volume of  $>250$  mL.

**Exclusion criteria:** Patients with indwelling urethral catheterisation, suprapubic cystostomy, previous bladder surgeries, concomitant urethral strictures and sonographic evidence of bladder diverticuli. The cases taking medical treatment for BPH as well as patients who could not achieve and maintain bladder volume  $>250$  mL were excluded.

Patients were evaluated with a validated IPSS questionnaire [14, 15] and a structured proforma containing demographic data, relevant history, clinical examination findings and investigation results. The DWT was then measured transabdominally on all the patients using real-time ultrasound scanner (Aloka Prosound SSD- 3500SX TM,

Tokyo, Japan) with a 3.5 MHz transducer ultrasound probe. Each patient was then instructed to drink plenty of water until first intense urge to void was experienced. The bladder volume was measured sonographically and documented. All the DWT measurements in this study were done at bladder filling  $>250$  mL to ensure reproducibility. Having ensured that bladder volume is  $>250$  mL and with adequate magnification, the adventitia, detrusor and mucosa were clearly identified. The DWT was then measured with electronic caliper for each patient at three different anatomical sites (dome, anterior and lateral walls) of the bladder. To increase the accuracy of the measurements, the average value of the DWT was then calculated (i.e., anterior DWT+lateral DWT+dome DWT/3) for each patient and was then used for further data analysis. The prostate volume was calculated using ellipsoid formula (length $\times$ width $\times$ height $\times 0.52$ ) which has already been programmed into the ultrasound machine. As ultrasonography is observer-dependent, measurements were done only by the Consultant Radiologist as a member of the research group. Measurements done by one person without check and balances from another person is prone to bias. However, blinding of the measurer from the patients' characteristics was done in the present study to limit bias.

## STATISTICAL ANALYSIS

Data collected were analysed with SPSS version 20 (IBM; SPSS, Chicago, IL, USA). Results obtained were expressed using tables and figures where necessary. Frequencies and proportions were used to calculate descriptive statistics for discrete variables while the mean and standard deviation were used to quantitative variables. Paired-Samples t-test was used to determine whether mean differences between the measurements were statistically significant. Spearman's correlation was used to assess the correlation between DWT and IPSS. The p-value  $<0.05$  was considered significant.

## RESULTS

The mean age of patients in this study was 71.02 $\pm$ 9.10 years with the peak age range of 70 to 79 years [Table/Fig-1]. The duration of symptom ranged from 3 to 120 months with mean of 30.63 $\pm$ 26.60 months. The IPSS ranged from 10 to 32 with mean of 20.94 $\pm$ 6.13 and the majority of the respondents had IPSS in the range 16-20 [Table/Fig-2]. A total of 43 patients and 57 patients had moderate (IPSS=8-19) and severe (IPSS=20-35) LUTS respectively. None of the patients had mild LUTS (IPSS=0-7). The QoL score ranged from 1 to 6 with mean of 4.08 $\pm$ 1.08 with the majority (52%) of the patients having QoL score of 5.

Age range (years)	Frequency	Percentage (%)
40-49	1.00	1.00
50-59	6.00	6.00
60-69	31.00	31.00
70-79	50.00	50.00
80-89	10.00	10.00
90-99	2.00	2.00
Total	100.00	100.00

[Table/Fig-1]: Age distribution of the patients.

IPSS range	Frequency	Percentage (%)
6-10	2.00	2.00
11-15	21.00	21.00
16-20	27.00	27.00
21-25	23.00	23.00
26-30	22.00	22.00
31-35	5.00	5.00
Total	100.00	100.00

[Table/Fig-2]: Distribution of International Prostate Symptom Scores (IPSS) of the patients.

The prostate biopsy histopathologic diagnosis was BPH in 56 patients, adenocarcinoma in 33 patients while 11 patients had chronic prostatitis as the underlying causes of prostate-related BOO/LUTS.

The mean bladder volume at which the DWT measurements were done was 318.81±6.13 mL. The mean value for the anterior, lateral and dome DWT were 4.95±2.36 mm, 4.96±2.37 mm and 5.02±2.34 mm respectively while the average DWT measurements was 4.97±2.35 mm [Table/Fig-3].

Parameters	Mean±SD	Range
Age (years)	71.02±9.10	48.00-95.00
Symptom duration (months)	30.63±26.60	3.00-120.00
Prostate volume (mL)	116.49±75.19	12.19-413.10
Serum PSA (ng/mL)	55.44±47.11	1.90-172.00
Anterior DWT (mm)	4.95±2.36	1.40-13.10
Lateral DWT (mm)	4.96±2.37	1.40-13.10
Dome DWT (mm)	5.02±2.34	1.60-13.30
Average DWT (mm)	4.97±2.35	1.53-13.13
Bladder volume (mL)	318.81±6.13	251.00-450.20
IPSS	20.94±6.13	10.00-32.00
QoL Score	4.08±1.08	1.00-6.00

[Table/Fig-3]: Relevant statistical parameters of the study.

The mean difference between the anterior wall DWT and dome DWT measurements ( $P=0.009$ ), and that between the lateral wall DWT and dome DWT measurements ( $P=0.017$ ) were both statistically significant ( $p<0.05$ ). However, the mean difference between the anterior wall DWT and lateral wall DWT measurements ( $P=0.812$ ) was not statistically significant ( $p>0.05$ ) using paired sample t-test. A total of 97 patients had DWT  $\geq 2$  mm with the majority (53.00%) of them within the range of 3-4.99 mm [Table/Fig-4].

Average DWT range (mm)	Frequency	Percentage (%)
1-2.99	9.00	9.00
3-4.99	53.00	53.00
5-6.99	16.00	16.00
7-8.99	10.00	10.00
9-10.99	9.00	9.00
11-12.99	2.00	2.00
13-14.99	1.00	1.00
Total	100.00	100.00

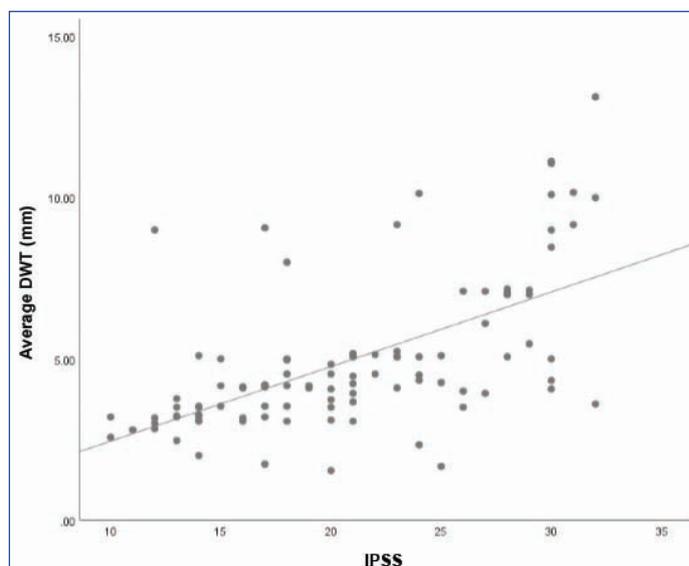
[Table/Fig-4]: Distribution of the average Detrusor Wall Thickness (DWT) measurements.

The average DWT correlated positively with the IPSS with Spearman's correlation coefficient  $r^2=0.635$  and  $p<0.001$ . The scatter plot also showed linear relationship between the average DWT and IPSS [Table/Fig-5].

## DISCUSSION

Prostate-related BOO/LUTS with consequent bladder wall changes are common in elderly men with the incidence increasing with the age [28]. The mean age of patients in this study was 71.02±9.10 years. In contrast, Bock-Oruma AA et al., in their study of incidence of BPH in Port Harcourt, South Nigeria, gave the mean age of 62.00±11.66 years [29]. However, Ogunbiyi JO et al., in their study of the incidence of prostate cancer in Nigeria gave the mean age of 71.4 years (variance 14.3) [30]. This is similar to mean age observed in the present study. Similar mean ages of 62.31±7.96 years and 61.7±9.2 years were noted by Kamyar E et al., in Iran and Yilmaz A et al., in Turkey, respectively [21,31]. The mean ages in these three studies were similar but at variance with the mean age recorded in our study [21,29,31].

The differences in mean age may be attributed to variations in the composition of the study population. The study included men



[Table/Fig-5]: Scatter plot showing linear relationship between the average Detrusor Wall Thickness (DWT) and International Prostate Symptom Scores (IPSS).

with LUTS secondary to both BPH and prostate cancer. From available epidemiological data, prostate cancer is known to have its peak incidence at a relatively higher age group than BPH [30]. Considering that a significant proportion of about 33% of patients had histopathologic diagnosis of prostate cancer in this study, it is not surprising that the observed mean age is similar to that noted by Ogunbiyi JO et al., [30]. On the other hand, the studies by Kamyar E et al., in Iran, Bock-Oruma AA et al., in Nigeria and Yilmaz A et al., in Turkey involved men with diagnosis of BPH, hence the lower mean age seen in these three studies compared to mean age reported in the present study [21,29,31]. The mean prostate volume of 116.49±75.19 mL was seen in this study. This is in contrast with the mean prostate volume of 53.54±35.31 mL noted by Yilmaz A et al., [31]. Delay in presentation for treatment in our environment and racial-related variations in prostate volume may account for higher prostate volume seen in Africans especially in our locality.

The mean bladder volume at which DWT measurements were done was 318.81±6.13 mL. Studies have shown that the DWT decreases rapidly during the first 250 mL of bladder filling and then remains relatively constant until maximum bladder capacity is reached [22,32]. Oelke M et al., recommends that the DWT should be measured at a full bladder or bladder filling volume of at least 250 mL [32]. Hence, all the DWT measurements in this study were done at bladder filling  $>250$  mL to ensure reproducibility. This is in keeping with work done by Kamyar E et al., and Yilmaz A et al., who also measured the DWT at bladder filling  $>250$  mL in their respective studies [21,31].

The mean anterior, lateral, dome and average DWT measurements were 4.95±2.36 mm, 4.96±2.37 mm, 5.02±2.34 mm and 4.98±2.35 mm, respectively. The study found that the mean difference between the anterior wall DWT and dome DWT, and that between the lateral wall DWT and dome DWT were both statistically significant ( $p<0.05$ ). However, the mean difference between the anterior wall DWT and lateral wall DWT measurements was not statistically significant ( $p>0.05$ ). Kojima M et al., reported that all parts of the bladder (anterior, posterior, lateral walls as well as the trigone and dome) have the same thickness in one individual [33]. This is at variance with the findings in this study which noted a slightly higher mean value of DWT measurement (5.02±2.34 mm) at the dome compared to mean of 4.95±2.36 mm and 4.96±2.37 mm recorded at anterior and lateral wall, respectively. Most studies on DWT measurements like the one by Kojima M et al., were done in western countries [33]. There is lack of similar studies comparing the measurement of DWT at different topographical regions of bladder wall in our environment. The finding of all parts of the bladder, not having same thickness, with measurements at the dome being significantly higher than that obtained elsewhere, opens up a window of opportunity

for further studies amongst black population especially in Nigeria as there may be some racial variations in such measurements.

Gabuev A and Oelke M, recommended that ultrasonic measurement of the DWT at the anterior bladder wall with filling volume  $\geq 250$  mL can accurately detect BOO at a value  $\geq 2$  mm [34]. This guided our choice of DWT of  $\geq 2$  mm as cut-off point of clinical relevance in DWT measurements. This study reported that 97% of the patients had DWT  $\geq 2$  mm. This is attributable to the fact that most of patients in our locality delay hospital presentation until symptoms become severe as depicted by the high average IPSS recorded in the present study.

The mean IPSS in the present study is  $20.94 \pm 6.13$  which falls within the severe symptom range. This is similar to mean IPSS of  $20.70 \pm 6.43$  reported by Yilmaz A et al., [31]; but at variance with the mean IPSS of  $14.60 \pm 5.00$  noted by Kamyar E et al., [21]. The severity of symptoms experienced by the patients in this study ranged from moderate to severe. Kamyar E et al., in their study also noted similar findings in the majority of their patients [21]. This is in contrast with the study by Bock-Oruma AA et al., who reported that 27.8%, 50.5% and 21.70% of respondents had mild, moderate and severe LUTS respectively [29]. This observed difference may be attributable to variations in study design, patient characteristics and selection. The observed predominance of moderate to severe symptoms with no mild symptoms in this study may be adduced to the habit of delay in seeking medical help in our locality. Patients often attribute their symptoms as part of normal ageing process thereby presenting late when the symptoms became very severe. Most of the patients were symptomatic with LUTS due to histopathologically proven BPH or prostate cancer which compelled them to present for clinical evaluation in the hospital. This is contrast with the prospective cross-sectional hospital based study by Bock-Oruma AA et al., which involved a wide spectrum of patients including apparently healthy ones [29]. Hence, their study had a significant number of patients with mild symptom compared to our study.

The high QoL score of 5 recorded in majority (52%) of the patients in the present study is also in keeping with the finding that all the patients presented with moderate to severe LUTS with significant negative impact on their QoL thereby compelling them to present to hospital.

In the present study, a significant correlation was found between the average DWT and IPSS ( $r^2=0.635$  and  $p<0.001$ ) which is in keeping with the findings from previous studies [16-18].

Oelke M et al., in assessing diagnostic accuracy of non invasive tests in evaluation of 160 men aged  $>40$  years with LUTS secondary to BPH found a statistically significant correlation between the DWT and IPSS ( $r^2=0.70$  and  $p<0.001$ ) [16]. Similarly, Casado SJ et al., in a prospective cross-sectional study of the correlation of the DWT with clinical and urodynamic data in 74 males with symptomatic BPH, also found a significant correlation between the DWT and IPSS ( $r^2=0.38$  and  $p=0.001$ ) [17]. Manieri C et al., in their study of 174 patients with LUTS secondary to prostate pathologies equally found a statistically significant correlation between the DWT and IPSS ( $r^2=0.60$  and  $p<0.007$ ) [18].

However, the work done by Yilmaz A et al., has demonstrated a weak positive but statistically insignificant correlation between the IPSS and DWT ( $r^2=0.023$ ,  $p=0.812$ ) [31] while Kamyar E et al., in their study, found no correlation between the pretreatment DWT and IPSS ( $r^2=0.0045$ ,  $p=0.9769$ ) [21]. The study done by Hakenberg OW et al., was equally at variance with the findings of this study and demonstrated a weak but statistically insignificant correlation between the DWT and IPSS ( $r^2=0.0075$ ,  $p=0.6728$ ) [22].

The finding of statistically significant correlation between the DWT and IPSS in this study and in the other similar previous studies [16-18] may be explained by the fact that prostate-related diseases with BOO, leads to LUTS with increased outlet resistance and IPSS

score. Unrelieved BOO with increase in the symptom score (IPSS) often leads to several structural, functional and biochemical changes in the detrusor muscle [4,6,10]. These changes often manifest as increase in ultrasound measured DWT. Therefore, as the degree of obstruction increases with increased IPSS, the DWT also increases. Hence, the strong positive correlation noted between the DWT and IPSS in this study and the previous ones [16-18]. On the other hand, a plausible explanation of the weak or even no correlation between the DWT and IPSS noted in some other studies [18,21,22] may be due to decompensatory changes in the bladder wall that may occur following protracted unrelieved BOO [35]. These decompensatory changes in bladder wall may lead to thinning of bladder wall and decrease in DWT with time despite progressive increase in symptom severity as assessed by the symptom score (IPSS). Hence, there may be no or even negative correlation between the DWT and IPSS in cases of protracted unrelieved BOO as has been shown in these studies [18,21,22].

However, these conflicting findings in the correlation between the DWT and IPSS reported by various researchers may also be due to variations in study designs and patient selection. Further studies are needed especially in our environment to further explore and validate these research findings. A larger sample-sized study in our environment might be needed for the findings of the research work to be generalised to a larger population.

### Limitation(s)

The ultrasonographic measurements of DWT were done manually which is subject to interobserver and intraobserver variability as opposed to automatic measurements. Hence, many researchers have proposed that the measurement of DWT should be done automatically instead of manually.

### CONCLUSION(S)

In conclusion, the finding of a strong positive correlation between the DWT and IPSS in this study has demonstrated that the DWT measurement can be used in assessing the severity of LUTS in men with prostate-related BOO/LUTS. With standardisation of the measurements, the DWT assessment holds a great deal of future hope and may likely in the near future replace other invasive tests in evaluation of patients with prostate-related BOO/LUTS.

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**PARTICULARS OF CONTRIBUTORS:**

1. Consultant Urologist, Department of Surgery, Alex Ekwueme Federal University Teaching Hospital Abakaliki, Ebonyi State, Nigeria.
2. Consultant Urologist and Senior Lecturer, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
3. Consultant Urologist and Lecturer, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
4. Consultant Radiologist and Senior Lecturer, Department of Radiology, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
5. Consultant Urologist and Professor, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
6. Consultant Urologist and Professor, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
7. Consultant Urologist and Professor, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
8. Consultant Urologist and Emeritus Professor, Department of Surgery, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Obasi Augustine Ulebe,  
Department of Surgery, Alex Ekwueme Federal University Teaching Hospital,  
P.M.B 102 Abakaliki, Ebonyi State-840001, Nigeria.  
E-mail: ulebester@yahoo.com

**PLAGIARISM CHECKING METHODS:** [Jain H et al.]

- Plagiarism X-checker: Jul 16, 2020
- Manual Googling: Jun 08, 2021
- iThenticate Software: Aug 10, 2021 (18%)

**ETYMOLOGY:** Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jul 15, 2020**  
Date of Peer Review: **Sep 03, 2020**  
Date of Acceptance: **Jul 12, 2021**  
Date of Publishing: **Sep 01, 2021**