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ORIGINAL RESEARCH

# Comparison of outcome of total versus subcapsular orchidectomy in the management of patients with advanced carcinoma of the prostate

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**Purpose:** The majority of patients in our environment present with advanced prostate carcinoma, necessitating hormonal ablation. Total and subcapsular orchidectomies are standard methods of hormonal ablation. This study aimed to compare the postoperative reduction in the levels of testosterone, prostate size, and patient satisfaction after total or subcapsular orchidectomy.

**Materials and methods:** This was a prospective hospital-based study. A total of 61 patients with advanced prostate adenocarcinoma were recruited into this study and randomised into either the total or subcapsular orchidectomy group. Serum testosterone assay and prostate volume estimation were done pre- and postoperatively. Complication rates and patient satisfaction with the procedures were determined and compared. Patients were followed up for three months. Data analysis used the Statistical Package for Social Sciences (SPSS) version 22. Results were displayed using appropriate statistical methods. For all statistical tests, $p < 0.05$ was significant.

**Results:** In the third month, the mean serum testosterone level of patients in the subcapsular group was statistically higher than that of patients in the total orchidectomy group ($p = 0.014$). There was no significant difference in the percentage of prostate volume reduction between the two groups at intervals of one ($p = 0.236$) and three ($p = 0.607$) months. There was also no difference in complication rate and outcome satisfaction between the two groups.

**Conclusion:** The higher mean testosterone of patients at three months in the subcapsular orchidectomy group raises concern about the long-term efficacy of subcapsular orchidectomy. This underlines the need for long-term follow-up.

**Keywords**: prostate carcinoma, total orchidectomy, subcapsular orchidectomy, serum testosterone, prostate size

## Introduction

Worldwide, prostate cancer is the most common male genital cancer.[1] Among black people, it has been described as a public health epidemic.[2] Various studies by eminent scholars in Nigeria have shown varying but relatively high incidence rates among Nigerians.[3-6] Most Nigerian studies reported late presentation among most prostate cancer patients with attendant poor prognosis.[7-9]

Prostate cancer may be palliated by androgen deprivation in patients with advanced disease or those for whom curative treatment for clinically localised disease has failed. Androgen deprivation may be provided through a variety of methods with equal efficacy; however, bilateral orchidectomy remains the least expensive.[10] Despite this, when given a choice, most patients choose medical androgen ablation, presumably due to the psychological consequence of losing their testes.[11] Consequently, various surgical procedures were designed to preserve "palpable testes". These include subcapsular orchidectomy, subcapsular orchidectomy with eversion of the tunica albuginea above the epididymis, implantation of testicular prosthesis, sub-epididymal orchidectomy, and orchidectomy in combination with a fibro-fatty graft to the tunica vaginalis.[12,13] These options did not gain general acceptance because of scepticism that they achieve castrate levels of testosterone/preserve significant testicular size.

In 1942, Riba et al. described the technique of subcapsular orchidectomy and advocated its use for the treatment of metastatic prostate cancer because it left palpable "testicles".[14] In 1958, subcapsular orchidectomy fell into disrepute when McDonald and Calams showed the presence of Leydig-like cells in the tunica albuginea and epididymis.[15] In 1963, O'Connor and associates showed that stimulation of patients who had undergone subcapsular orchidectomy produced a rise in the urinary excretion of testosterone metabolites.[16] Subsequent studies reported no differences in postoperative testosterone levels after total or subscapular orchidectomy.[17-19]

This study aimed to compare the effectiveness of total and subscapular orchidectomy in the management of patients with advanced prostate adenocarcinoma. Therefore, this study will provide local data on the outcomes of total and subcapsular orchidectomies in the management of advanced prostate carcinoma. This study may also form a scientific basis for counselling men with advanced prostate carcinoma who choose orchidectomy as a method of androgen deprivation.

## Materials and methods

This study is a prospective, comparative hospital-based study done over 18 months in a suburban teaching hospital in southern Nigeria. All patients with histologically confirmed prostate adenocarcinoma who consented to bilateral orchidectomy and had not commenced

any treatment for the disease were included in the study. Consecutive patients who fulfilled the inclusion criteria were enrolled into two study groups as they presented at the urology outpatient clinic. The study's objectives were explained to each patient during enrollment and informed consent was obtained. Simple randomisation with a coin flip was done to select the first participant's assigned treatment group. Subsequent consecutive patients were alternated between the two treatment groups as they presented. Group A was subjected to total orchidectomy, while group B was subjected to subcapsular orchidectomy.

A detailed clinical history was taken from all recruited patients, and a full physical examination was performed on each. Fasting serum testosterone was assayed for all patients using a DRG testosterone enzyme-linked immunosorbent assay (ELISA) kit (DRG Instruments, GmbH, Germany, division of DRG International Inc.).

The prostate volume of all patients was assessed using an abdominopelvic ultrasound scan. Skin preparation was done with Savlon thrice, followed by povidone-iodine. A sterile draping was then applied. Local anaesthesia was achieved by spermatic cord block using 8–10 ml 0.5% Xylocaine, local skin infiltration of incision site using 3–5 ml 0.5% Xylocaine, and a 3–4 cm long median raphe scrotal skin incision was made and deepened through the scrotal wall and testicular coverings to access the scrotal cavity. The testes, epididymis, and distal part of the spermatic cord were removed in the total orchidectomy group (group A). The cord stump was secured using Vicryl 1, and the artery was transfixed twice, separately from the veins.

In the subcapsular orchidectomy group (group B), the tunica albuginea was opened longitudinally along its bloodless border. The testicular content was removed followed by the closure of the tunica albuginea with a Vicryl 2-0 suture.

Haemostasis was fully secured. The wound was closed in two layers. Vicryl 2-0 was used to oppose the subdartos tissue, while simple skin closure was done using nylon 3/0. Pressure dressing and scrotal support were applied to prevent haematoma formation. Postoperative analgesia was achieved using oral 50 mg tramadol given twice daily for five days, prophylactic antibiotic coverage with 500 mg oral ciprofloxacin twice daily, and 400 mg oral metronidazole three times a day for five days.

A fasting blood sample was collected at 8 a.m. on postoperative day one, and after that, at one week, four weeks, and three months to assay the testosterone level using the DRG testosterone ELISA kit. The patients' wounds were inspected on the fifth postoperative day for any evidence of infection, such as undue tenderness, erythema, swelling, and discharges from the surgical site. The suspected wound infection was confirmed with a wound swab culture. The scrotum was inspected for haematoma formation. Reoperation was considered a complication.

All patients had abdominopelvic ultrasound prostate volume estimation repeated by the same sonologist at one and three months. At the three-month postoperative visit, each patient's satisfaction was assessed. Data collection was done using a pro forma designed for this study. All relevant information, including biodata, clinical, laboratory, and radiological findings were documented in the pro forma sheet.

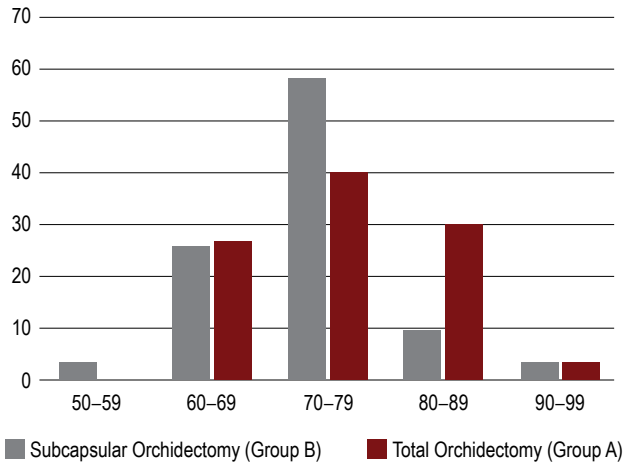


Figure 1: Age distribution of patients in both groups

The statistical analysis used the SPSS for Windows program (version 22, SPSS Inc., Chicago, Illinois). Differences between the groups were tested with the t-test. The level of significance was set at $p < 0.05$. The frequency distribution for the variables is presented in tables and charts.

## Results

The inclusion criteria were fulfilled by 61 patients recruited into the study. Of the patients, 30 had total orchidectomy (group A), and 31 had subcapsular orchidectomy (group B). The age range of the patients in group A was 61–92 years, while that of group B was 59–91 years. The mean age of patients in group A was 74.7 ± 7.9 years and 72.9 ± 6.4 years in group B. The age distribution of the patients in both groups is shown in Figure 1.

The range of serum prostate-specific antigen (PSA) of patients in group A was 8–150 ng/ml with a mean of 62.06 ng/ml, while group B had 13.5–158.2 ng/ml with a mean of 73.08 ng/ml. There was no statistically significant difference in serum PSA levels between the groups ($p = 0.316$). The mean Gleason score for patients in group A was 6.23 and 6.22 for group B. There was no statistically significant difference in the Gleason score between the groups ($p = 0.977$). Therefore, the two groups are considered comparable. Table I shows that the serum testosterone decreased to castrate levels in both groups until three months post-intervention.

Table I: Mean serum testosterone levels of patients pre- and post-orchidectomy

| Groups | Mean testosterone (ng/ml) | | | | |
|---|---|---|---|---|---|
| | Pre-op | POD 1 | POD 7 | 1 month | 3 months |
| A | 6.97 | 0.44 | 0.35 | 0.25 | 0.16 |
| B | 7.01 | 0.46 | 0.38 | 0.33 | 0.29 |

POD – postoperative day

The greatest postoperative percentage reduction in prostate volume was at one month. The postoperative percentage prostate volume

reduction at one and three months for group A were 35.88 and 57.37, respectively, and for group B, 39.90 and 58.65, respectively (Table II).

**Table II:** Mean percentage reduction in prostate volume of patients at intervals of one and three months post-orchidectomy

| Groups | Mean prostate volume reduction (%) | |
|---|---|---|
| | 1 month | 3 months |
| A | 35.88 | 57.37 |
| B | 39.90 | 58.65 |

Table III shows no statistically significant difference between the two groups' preoperative serum testosterone levels. There was no significant difference in postoperative serum testosterone levels on day one, at one week, and one month. However, at three months, the serum testosterone levels were higher in the subcapsular orchidectomy group. This was statistically significant ($p$ = 0.014).

**Table III:** Comparison between serum testosterone levels of patients in both groups

| Serum testosterone (ng/ml) | Group A | | Group B | | |
|---|---|---|---|---|---|
| | Range | Mean | Range | Mean | p-value |
| Pre-op | 0.7–13.4 | 6.97 | 3.3–12.2 | 7.01 | 0.146 |
| Post-op | | | | | |
| 1 day | 0.1–0.9 | 0.44 | 0.1–0.9 | 0.45 | 0.804 |
| 1 week | 0.2–0.9 | 0.35 | 0.2–0.9 | 0.38 | 0.763 |
| 1 month | 0.0–0.6 | 0.25 | 0.1–1.3 | 0.33 | 0.145 |
| 3 months | 0.1–0.7 | 0.16 | 0.1–1.0 | 0.29 | 0.014 |

Table IV shows that there was no statistically significant difference in the percentage reduction in prostate volume at one and three months between the two groups. Both groups had four patients with complications. Three patients in each group had wound infection, while one in each group had scrotal haematoma. There was no statistical difference between the two groups ($p$ = 0.922).

**Table IV:** Comparison between the reduction in prostate volume in both groups

| % Reduction Volume | Group A | | Group B | | |
|---|---|---|---|---|---|
| | Range | Mean | Range | Mean | p-value |
| Post-op | | | | | |
| 1 month | 8.5–72.7 | 35.88 | 8.3–77.6 | 39.90 | 0.330 |
| 3 months | 23.1–81.3 | 57.37 | 35.0–81.3 | 58.67 | 0.704 |

When asked about their overall feeling regarding the mode of treatment for their condition, 21 (70.0%) patients in group A felt very satisfied, and 9 (30.0%) felt satisfied. In group B, 18 (58.1%) were very satisfied, and 13 (41.9%) were satisfied. None in each group felt indifferent, dissatisfied, or very dissatisfied (Figure 2). There was no statistically significant difference in the satisfaction levels between the two groups ($p \leq 0.382$). The responses to questions on the bothersomeness of the change in scrotal size and procedure recommendation to another patient were similar in both groups.

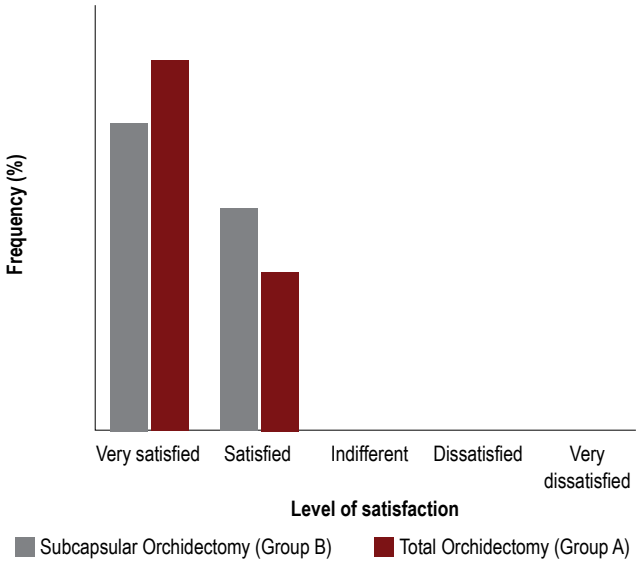


**Figure 2:** Level of satisfaction with treatment in both groups

## Discussion

There is currently no curative therapy for advanced prostate carcinoma. Treatment is aimed at palliation. About 80% of these cancers are androgen-dependent at the time of diagnosis; thus, the disease progression can be controlled by androgen deprivation.[20] Androgen deprivation, the cornerstone for the treatment of advanced prostate cancer, can be achieved with bilateral total orchidectomy or using a luteinising hormone-releasing hormone (LHRH) agonist or antagonist. Both methods have been shown to have similar therapeutic effects, but there are differences in the cost of the latter, as well as psychological and cosmetic issues with the former.

Clinical studies have suggested that surgical orchidectomy is superior to medical therapy because it more rapidly achieves castrate levels of serum testosterone, avoids the testosterone flare, is less expensive, and has superior therapeutic compliance.[21,22] However, total orchidectomy as a treatment modality for advanced prostate adenocarcinoma has become unpopular in many places due to patients' concern about body self-esteem and appearance, as well as the ingrained societal aversion to castration.[23,24] Consequently, a castration method that does not adversely affect male appearance and self-image would be a good alternative. Subcapsular orchidectomy has been reported to achieve these outcomes.[25]

The findings from this study show that the two groups are comparable because there was no statistically significant difference in the Gleason score ($p$ = 0.977) and serum PSA ($p$ = 0.316). The preoperative testosterone levels ($p$ = 0.146) and prostate volume ($p$ = 0.051) showed no significant difference between the two groups. Therefore, a reasonable conclusion can be drawn from the study without bias. The mean total testosterone values for patients who had total and subcapsular orchidectomy in this study were in the castrate range and remained there after the three-month follow-up. Furthermore, the mean total testosterone levels in both groups were comparable on day one, at one week, and one month.

After bilateral total orchidectomy, serum testosterone is produced through the conversion of adrenal dehydroepiandrosterone by 3-beta hydrosteroid dehydrogenase and from the conversion of adrenal androstenedione through 17-beta hydroxysteroid dehydrogenase. Both adrenal steroids are regulated by adrenocorticotropic hormones, and their levels do not increase following bilateral orchidectomy.[26] Several studies have shown that the mean total testosterone level following bilateral total orchidectomy is 0.5 ± 0.5 ng/ml, and there is no late rise in plasma testosterone levels.[27,28]

The main rationale behind the use of bilateral orchidectomy in the management of advanced prostate adenocarcinoma is to bring the serum testosterone value below the castrate level. Several studies have confirmed the comparable effect of both methods in lowering the levels of testosterone and concluded that subcapsular orchidectomy is as effective as total orchidectomy in the management of prostate adenocarcinoma.[19,29,30]

At three months of follow-up, the testosterone levels of patients who had subcapsular orchidectomy, though within the castrate range, were statistically higher than those of the patients who had total orchidectomy ($p$ = 0.014). Leydig cells have been demonstrated to be morphologically present in the tunica albuginea and epididymis, both structures that are left behind in subcapsular orchidectomy.[15] Nonetheless, they lack the capacity to regenerate or produce endocrine function. Senge et al. corroborated this when they reported no rise in testosterone levels in patients up to eight months after subcapsular orchidectomy.[31] This view was supported in the study by Vermeulen et al., wherein bilateral subcapsular orchidectomy also produced testosterone levels in the castrate range.[32] There was no evidence of reactivation of Leydig cells or increased adrenal androgen secretion as evaluated from plasma testosterone and androstenedione sulphate levels during the year following subcapsular orchidectomy.

It is possible that the scattered Leydig cells in the tunica albuginea and epididymis contributed to the higher serum testosterone levels observed in the patients who had subcapsular orchidectomy after three months in this study. Production of testosterone by the scattered Leydig cells in the tunica albuginea and epididymis has been previously documented.[15]

Because of the observed difference in the mean total testosterone at three months between the two groups, patients should be offered subcapsular orchidectomy with caution. There is a need for follow-up beyond three months post-subcapsular orchidectomy. However, it should be noted that the serum testosterone levels remained within the castrate range in both groups of patients even at the three-month follow-up.

There was a reduction in prostate volume after orchidectomy in both groups. Reduction in prostate volume and subsequent improvement in urinary symptoms have been documented following bilateral orchidectomy.[31,33] Androgenic steroids are required to maintain the prostate gland in the adult state. Androgen deprivation therapies typically induce a drastic regression of mature prostate tissue, accompanied by the extensive loss of prostate cells through the programmed cell death process referred to as apoptosis.[33]

Other pathological mechanisms thought to be responsible for the regression of prostate tissue following androgen deprivation include:

1. loss of cells due to the direct response of the cells to an androgen-depleted environment; and
2. initiation of an indirect response of the prostate parenchyma to an ischaemic/hypoxic environment caused by a marked reduction of blood flow to the tissue that occurs when androgens are withdrawn.[33]

In both groups, the greatest volume reduction was observed during the first month after castration. A similar observation was made by Zdrojowy when he evaluated changes in prostatic volume in 84 men with prostate adenocarcinoma treated with bilateral orchidectomy.[34] The initial decrease in volume of the primary tumour seems to be a critical parameter for predicting progression or stability in patients treated with bilateral orchidectomy. There was no statistically significant difference between the percentage reductions of prostate volume in the two groups at all intervals of the study. This finding suggests that subcapsular orchidectomy has comparable efficacy with total orchidectomy in reducing prostate volume.

Bilateral orchidectomy is a proven method of androgen deprivation with good oncological efficacy. It is simple, inexpensive, and induces rapid relief from cancer symptoms. Nevertheless, it can be associated with some minor postoperative complications. In this study, four patients in each group had minor surgical complications that were easily managed. Three patients in each group had superficial surgical site infections, which were successfully managed with wound dressings. The pattern of complications observed in this study is similar to that reported by others.[24,34] There was no statistically significant difference in the postoperative complication rate between the two groups ($p$ = 0.922), as documented in the literature.[35] This finding suggests that subcapsular orchidectomy is comparable to total orchidectomy in the rate of postoperative complications.

There was no significant difference in patients' satisfaction with the treatment outcome between the two groups ($p$ = 0.382). No patient in either group was bothered about the change in the size of the scrotum. Moreover, all patients in both groups showed a willingness to recommend the procedure to another person with a similar condition. This observation is contrary to what is known and documented earlier. It is well documented that bilateral orchidectomy is a less preferred method of androgen deprivation owing to the alteration in body image and the associated psychological trauma.[11] On the contrary, subcapsular orchidectomy is said to be associated with better patient satisfaction because the body image is preserved.[24,27]

The findings in this study could be partly attributed to the preoperative counselling and the good clinical improvement achieved in both groups, which overshadowed any perception of alteration in body image or psychological trauma. Another explanation could be that patients in this study may have considered an alteration in scrotal size or complete loss of testes a lesser problem compared to the possibility of loss of life. Finally, it has been documented that bilateral orchidectomy does not affect self-concept.[35,36,37] This study suggests

that subcapsular orchidectomy is comparable to total orchidectomy in testosterone reduction, prostate volume reduction, complication rate, and patient satisfaction with the treatment outcome.

### *Study limitations*

The short-term evaluation and the small sample size are limitations to the conclusion regarding the effectiveness of the treatment methods.

### *Study strengths*

This study determined the percentage reduction in prostate volume following total and subcapsular orchidectomy and compared the difference in this outcome between the two procedures. Previous studies that compared the efficacy of these two procedures did not assess prostate volume reduction.

## Conclusion

Subcapsular orchidectomy, as an option in the management of advanced prostate adenocarcinoma, is as effective as total orchidectomy in reducing serum testosterone to castrate levels. Patients should be informed about the equal efficacy of both orchidectomy methods in managing their condition. Those who choose subcapsular orchidectomy should be informed of the possibility of a rise in testosterone in the future and that the consequence of this is not clear. Due to the higher mean testosterone at three months in patients who had subcapsular orchidectomy, there is a need for long-term studies on follow-up in patients who had either bilateral total or subcapsular orchidectomy to determine the long-term efficacy.

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### *Conflict of interest*

The authors declare no conflict of interest.

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### *Ethical approval*

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