

Review Of The Adverse Effects Of Radiation Therapy Seen In Men After Treatment For Prosate Cancer In A Tertiary Health Centre In Aba, South Eastern Nigeria.

Ibe U. Ibe

*Consultant Urologist
Department Of Surgery,
Abia State*

University Teaching Hospital, Aba Nigeria

John Austin Chikezie

*Consultant Nephrologist
Department Of Internal Medicine
Abia State University Teaching Hospital, Aba Nigeria*

Obinna Chikezie,

*Medically Officer
Department Of Medical Services
Abia State Ministry Of Health,
Umuhia, Abia State Nigeria*

Abstract

Prostate cancer is the most common cancer in nigeria with increasing morbidity and mortalities.

Radiation therapy is a major modality of management.

Radiation therapy is used in the management of organ confined prostate cancer with both low and high risks. It is used in locally advanced disease and in disease recurrence after radical prostatectomy. It is also used on palliative basis for metastatic prostate cancer.

Useful as it is in the management of various stages of prostate cancer, it produces deleterious effects to the body.

The aim of the study was to retrospectively review the pattern of occurrence adverse effects seen in men managed with radiation therapy over an 8 year period from january 2015 to december 2022.

Of the 202 men who had histopathologically confirmed prostate cancer within the period of study, only 115 (56.9%) had radiation therapy at one stage in their management.

All these 115 men had external beam radiotherapy. The most common adverse effect was diarrhea seen in 54 men (47%) followed by nausea and vomiting seen in 48 men (41.7%). This was followed by a peculiar dermatitis located on the suprapubic region. It was seen in 40 men (34.8%). Other adverse effects were obstructive voiding seen in 30 men (26.1%) and rashes seen in 25 men (21.7%).

Haematochezia and urethral stricture were rare occurrences. Haematochezia was seen in only 1 man (0.87%) while incomplete urethral stricture was also seen in 1 man (0.87%).

Lymphoedema of the genital and urethral stricture was seen after 12 months of exposure.

Gastrointestinal adverse effects were the most common seen in aba, nigeria.

Key words: *Prostate cancer, radiation therapy, adverse effects and aba.*

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I. Introduction

Radiation therapy is a most useful management protocol for most cancers. It is particularly useful in the management of prostate cancer. Radiation therapy is used in the management of organ confined prostate cancers especially in the low risk group.

Cure rate for these men are about the same as men treated with radical prostatectomy.

It is used in:

- ❖ Organ confined high risk cancers.
- ❖ Locally advanced prostate cancer, radiation is the mainstay of treatment along with neo adjuvant and adjuvant hormonal therapy.
- ❖ It is found very useful in recurrence of the disease after radical prostatectomy.
- ❖ It is also used in the palliative setting in metastatic prostate cancer. Palliative radiation therapy is given using fewer doses than curative radiotherapy.

It does not aim to cure the cancer but:

- Slows down cancer growth and progression
- To control the symptoms caused by the cancer such as pains.

In the palliative setting, it is used to:

- ❖ Shrink the tumor
- ❖ Stop bleeding if any.
- ❖ Treating spinal cord and nerve compressions
- ❖ Relief of bone pains

As comprehensively useful as radiation therapy is, it is accompanied by adverse effects occurring during and after the radiation process.

The adverse effects are due to the untoward effects of radiation on normal tissues surrounding or near the target organ.

There are basically three (3) main types of radiation therapy:

1. External beam radiotherapy
2. Internal beam radiotherapy otherwise called brachytherapy
3. Radiopharmaceuticals where radioactive substances are injected into the body to release radiation internally.

The adverse effects of radiation occur due to the following factors:

- ❖ The area of the body radiated.
- ❖ The type of cancer.
- ❖ The dose of radiation given.
- ❖ The duration of exposure.
- ❖ Host immunity and co-morbidities

In order to prevent or reduce the occurrence of the adverse effects, many variations of the three main types of radiotherapy had been developed all aimed at little or no exposure of radiation to normal tissues.

The external beam radiotherapy has several variants:

3 dimensional conformal radiotherapy (3 d-crt).

It uses special computers to map out the prostate

Intensity modulated radiotherapy (imrt).

It is an advanced form of 3d-crt which rotates round the patient delivering radiation to the prostate from several angles. A variant of this is called volumetric modulated arc therapy (vmat). It delivers radiation much quicker than conventional imrt.

Stereostactic body radiation therapy (sbrt):

It uses advanced image guided techniques to deliver large doses of radiation to a precise area of the prostate.

Mri guided radiation therapy:

This combines 3d-crt and imrt and image guided techniques in one.

Proton beam radiation therapy:

It focuses a beam of protons on the target tissues instead of x-rays (photons) used by other methods.

Photons or x-rays release their energy before and after hitting their target and may therefore inflict damage on surrounding normal tissues. But protons release their energy after travelling a distance and hitting their target making them less able to cause damage to normal tissues.

Hyperfractionation techniques:

This is a technique used to deliver high doses of radiation over a short period so as to reduce the duration of exposure.

Brachytherapy on the other hand has 2 major variants, it is called seed implantation or interstitial radiation therapy. It is used in:

- ❖ Early stage cancer especially low risk type.
- ❖ Use in combination with external beam radiotherapy whenever risk is high.

It is achieved with the implantation of radioactive seeds unto the prostate after imaging tests.

Variants include:

- Permanent (low dose rate) brachytherapy
- Temporary (high dose rate) brachytherapy

All these measures are instituted to reduce the occurrence of adverse effects and making radiotherapy a safer and effective modality of treatment. But despite all these, some adverse effects still occur.

II. Methodology

This was a retrospective study of men who received radiation therapy as a modality of management of prostate cancer over an 8 year period from January 2015 to December 2022. Those men were followed up over the years after radiation therapy. Their case files were withdrawn and important information obtained including age, treatment modalities instituted, adverse effects following exposure and the treatments given.

All the 115 patients had external beam radiotherapy.

Inclusion criteria

All men seen within the study period with histopathologically confirmed prostate cancer who had radiation therapy at one stage in their management were part of this study.

Exclusion criteria

All men with histopathologically confirmed prostate cancer within the study period who had no radiation therapy were excluded.

III. Results

Patients were aged between 40 to 100 years, median age was 65 and mean age was 69.5 years (variance=6.9) + or _3sd.

Patients suffered more than one form of adverse effects. Only 115 men out of 202 with prostate cancer – adenocarcinoma (56.9%) had radiation therapy within the period.

Diarrhea was found to be the most common adverse effect as it was seen in 54 men (47%) closely followed by nausea and vomiting seen in 48 men (41.7%) and then suprapubic dermatitis in 40 men (34.8%).

Haematochezia and incomplete urethral stricture were very rare and were seen in only one man (0.87%) in each case.

Lymphoedema of the scrotum and urethral stricture were seen after 12 months of exposure.

Table 1 – showing age group/range characteristics of all histopathologically confirmed prostate cancers (adenocarcinoma)

S/n	Age group	Number	Percentage
1.	40 – 50 years	3	1.5%
2.	51 – 60 years	16	7.9%
3.	61 – 70 years	74	36.7%
4.	71 – 80 years	78	38.6%
5.	81 – 90 years	28	13.9%
6.	91 – 100 years	3	1.5%
7.	Total	202	100%

Table 2 – age group/range characteristics of all histopathologically confirmed adenocarcinomas managed by neo – adjuvant hormonal treatment and radiation therapy

S/n	Age group	Neo adjuvant hormonal therapy	Radiation therapy
1.	40 – 50 years	2	1
2.	51 – 60 years	15	10
3.	61 – 70 years	51	40
4.	71 – 80 years	60	52
5.	81 – 90 years	24	12
6.	91 – 100 years	3	Nil
	Total	155	115

Table 3 – showing the use of radiation therapy at different stages of the prostate cancer

S/n	Clinical stage	Hormonal Therapy	Radiation therapy
1.	Metastatic stage	120	82
2.	Locally advanced stage	30	29
3.	Organ confined stage	5	4
	Total	155	115

Table 4 – showing the adverse effects of radiation therapy and their percentage occurrence

S/n	Adverse effects	Number	Percentage
1.	Diarrhea	54	47%
2.	Nausea and vomiting	48	41.7%
3.	Dermatitis (often thickened skin at suprapubic region)	40	34.8%
4.	Obstructive voiding	30	26.1%
5.	Rashes at genital area and buttocks	25	21.7%
6.	Radiation cystitis	20	17.4%
7.	Fatigue	18	15.7%
8.	Temporary erectile dysfunction	15	13%
9.	Pubic hair loss	8	7%
10.	Lymphoedema of scrotum	5	4.3%
11.	Haematochezia	1	0.87%
12.	Incomplete urethral stricture	1	0.87%

Fig 1.

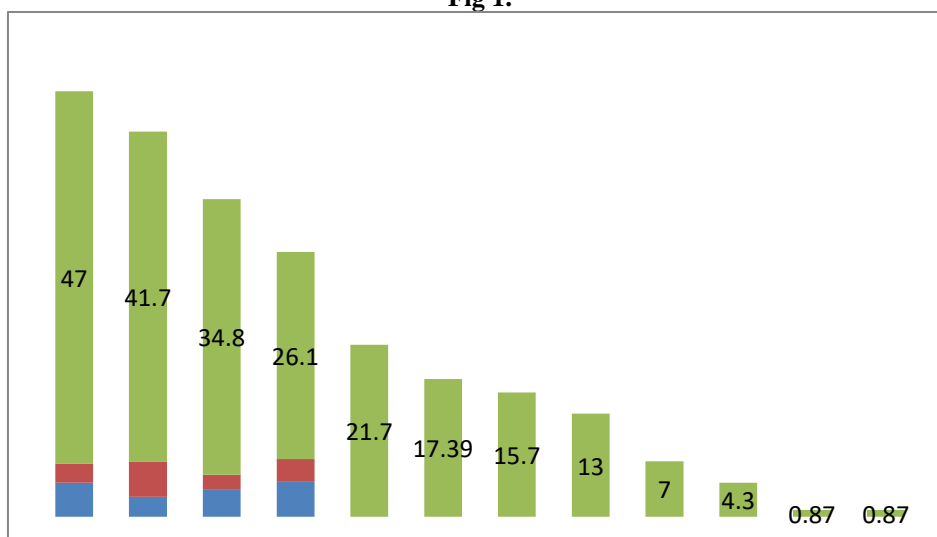


Table 5 – showing time lag from radiation exposure to onset of development of adverse effects

S/n	Adverse effects	From one to few weeks post exposure	More than 6 months post exposure	More than 1 year post exposure
1.	Diarrhea	Yes		
2.	Nausea and vomiting	Yes		
3.	Dermatitis (often thickened skin at suprapubic region)		Yes	
4.	Obstructive voiding	Yes		
5.	Rashes at genital and buttocks	Yes		
6.	Radiation cystitis	Yes		
7.	Fatigue	Yes		
8.	Temporary erectile dysfunction		Yes	
9.	Pubic hair loss		Yes	
10.	Lymphoedema of the scrotum			Yes
11.	Haematochezia	Yes		
12.	Incomplete urethral stricture			Yes

IV. Discussion

Radiotherapy is the chief non-surgical modality to control malignant tumors.

It has advanced methodology, techniques and biological aspects in the past few years.

Although radiation therapy is a useful adjunct and non-invasive, still it leaves behind some deleterious adverse effects which are classified as:

- Early effects
- Consequential effects and
- Late effects

Acute or early radiation toxicity is seen within a few weeks of commencement of radiation therapy and usually involves rapidly dividing cells such as the skin and mucosa.

Consequential effects are seen when acute effects are not treated and cause persistent damage.

Late effects occur after months to years of radiation exposure.

These are seen in slow dividing cells such as liver, kidney, heart and skeletal muscle.

Consequences of radiation in slow growing tissues include:

- Fibrosis
- Vascular damage
- Complex interplay of cytokines and cellular processes

Damage results in:

- Increased permeability
- Subsequent release cytokines – beta tgf and fibrin promoting collagen deposition

Most of the organs have threshold doses of radiation above which late effects increase.

Leucocyte adhesion to damaged endothelial cells results in the formation of thrombin and subsequent distal ischemia resulting in necrosis.

Further cell loss may trigger and perpetuate the cytokine storm and cellular interactions.

Radiation injury results from interplay of factors:

- Radio biologic factors
- Intrinsic radio sensitivity
- Volume of tissue radiated
- Dose of radiation given
- Dose per fraction
- Duration of exposure
- Type of cancer
- Location of the organ

- Combination of surgery and chemotherapy
- Associated co-morbidities

Various adverse effects seen in radiation therapy for prostate cancer include:

- Diarrhea
- Nausea and vomiting
- Dermatitis
- Obstructive voiding
- Rashes
- Urinary incontinence
- Radiation proctitis
- Rectal bleeding
- Haematochezia
- Radiation cystitis
- Fatigue
- Lymphoedema
- Erectile dysfunction
- Urethral stricture

Our study was similar to the work done by Ulla Sisko Lehto et al, in 2017 on patients' perceptions of the negative effects following different prostate cancer treatments and the impact on psychological wellbeing.

It was a comprehensive study of the negative effects of treatment modalities instituted in the management of prostate cancer including radical prostatectomy, hormonal treatment, chemotherapy and radiation therapy.

They conducted a nationwide survey that included 1239 men with detailed information regarding the negative effects and the occurrence, perceived level and perceived bother since the beginning of treatment. Furthermore, they measured patient satisfaction with the treatment outcome and their psychological wellbeing. They found out that radiotherapy caused urinary leakage, symptoms of urinary irritation and bowel dysfunction. Most symptoms were considered bothersome enough to give poor psychological outcome.

V. Conclusion

Bowel, skin and urinary adverse effects were the leading negative effects of radiation therapy seen at Aba. The dreaded complications of urethral stricture, impotence and infertility were not found to be common.

Radiation therapy is a most useful adjuvant in the management of prostate cancer but comprehensive counseling of the patients is necessary before institution of the therapy.