







ORIGINAL

## Assessment of Bone Mineral Density Decline in Prostate Cancer Patients Undergoing Hormonal Therapy

### Evaluación de la disminución de la densidad mineral ósea en pacientes con cáncer de próstata sometidos a terapia hormonal

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#### ABSTRACT

**Introduction:** the prostate cancer is a highly prevalent cancer in men, and enhanced screening and treatment have helped in earlier detection and greater longevity. However, due to complications, patients' quality of life has grown more crucial. Despite regional therapy, Prostate cancer naturally develops to metastasis, notably in the bone, increasing mortality and morbidity from skeletal-related events and necessitating operation or therapy. The objective of the article is to analyze the influence of various hormone therapies on bone mineral density, termed Bone Mineral Density(BMD) in individuals with prostate cancer.

**Method:** the research includes two groups, in Group A patients who have prostate cancer take the treatment named Luteinizing Hormone-Releasing Hormone agonists (LHRH), and for Group B patients, the treatment called anti-androgen hormonal therapy. It particularly analyses the impact of LHRH in Group A on anti-androgen medication in Group B.

**Results:** a questionnaire was presented to the patients to gather data on several parameters such as medical information, and lifestyle behaviors. A paired t-test and multiple linear regression analyses were carried out using the SPSS software version 28, to investigate the impact of hormonal treatment on BMD results.

**Conclusions:** the research found that age, duration of hormone therapy, BMI, and baseline BMD were significant indicators of BMD changes among patients with prostate cancer. The results suggest that group A, which was undergoing LHRH treatment, is more successful in maintaining BMD, compared to the group B, which emerged from anti-androgen therapy.

**Keywords:** Prostate Cancer; Medical Care; Hormonal Therapy; Bone Wellness; Risk Factors.

#### RESUMEN

**Introducción:** el cáncer de próstata es un cáncer de alta prevalencia en hombres, y la mejora de las pruebas de detección y el tratamiento han contribuido a una detección más temprana y una mayor longevidad. Sin embargo, debido a las complicaciones, la calidad de vida de los pacientes se ha vuelto crucial. A pesar de la terapia regional, el cáncer de próstata desarrolla metástasis de forma natural, especialmente en el hueso,

lo que aumenta la mortalidad y la morbilidad por eventos relacionados con el esqueleto y requiere cirugía o tratamiento. El objetivo del artículo es analizar la influencia de diversas terapias hormonales en la densidad mineral ósea (DMO) en personas con cáncer de próstata.

**Método:** la investigación incluye dos grupos: el Grupo A, pacientes con cáncer de próstata que reciben el tratamiento con agonistas de la hormona liberadora de hormona luteinizante (LHRH), y el Grupo B, pacientes con terapia hormonal antiandrogénica. Se analiza en particular el impacto de la LHRH en el Grupo A sobre la medicación antiandrogénica en el Grupo B.

**Resultados:** se presentó un cuestionario a los pacientes para recopilar datos sobre diversos parámetros, como información médica y hábitos de vida. Se realizaron pruebas t pareadas y análisis de regresión lineal múltiple con el programa SPSS versión 28 para investigar el impacto del tratamiento hormonal en los resultados de la DMO.

**Conclusiones:** la investigación reveló que la edad, la duración de la terapia hormonal, el IMC y la DMO basal fueron indicadores significativos de los cambios en la DMO en pacientes con cáncer de próstata. Los resultados sugieren que el grupo A, que recibió tratamiento con LHRH, logró mantener la DMO con mayor éxito que el grupo B, que recibió terapia antiandrogénica.

**Palabras clave:** Cáncer de Próstata; Atención Médica; Terapia Hormonal; Bienestar Óseo; Factores de Riesgo.

## INTRODUCTION

People with cancer have a higher probability of rapid fractures even before begin cancer treatments, as demonstrated by decreased BMD in those with cancer compared to people without cancer, regardless of their disease type.<sup>(1)</sup> Adding to the inherent musculoskeletal discredit is the additional damage caused by several cancer medications. Thus, reduction of bone density in cancer patients illustrates both the effects of the cancer itself and the skeletal reaction to current cancer treatments such as chemotherapeutics, glucocorticoids, aromatase inhibitors (AIs), and androgen deprivation treatments.<sup>(2)</sup> Furthermore, bones are frequently the emphasis of cancer metastasis, with cells from tumors causing direct as well as indirect impacts on bone cells, resulting in systemic and localized bone damage.<sup>(3)</sup> When observed through the lens of higher longevity in patients with many forms of cancers, attempts to restrict bone loss and broken bones, which can dramatically reduce their quality of life, are growing increasingly crucial for cancer treatment of patients.<sup>(4)</sup> Prostate cancer is a very frequently identified male cancer in advanced nations. However, the prostate cancer has one of the greatest survival rates of any cancer with improved detection and therapy.<sup>(5)</sup> Androgen deprivation therapy (ADT) is commonly used to treat localized and metastatic prostate cancer in men. When administered correctly, it effectively controls Prostate cancer progression and improves overall survival rates.<sup>(6)</sup> ADT-induced hypogonadism can negatively impact cardiovascular, metabolic, sexual, and skeletal wellness. Cross-sectional studies have reported reduced dual-energy x-ray absorption (DXA) areal bone mineral density (aBMD) at different bone locations in ADT-treated males compared to those with Prostate cancer who did not receive treatment with ADT and older persons in excellent health, while others showed no significant difference.<sup>(7)</sup> When contrasted with typical age-related losses over time, males treated with ADT exhibit a fivefold increase in Abd reduction. There was research on the effects of ADT on bone strength measures other than aBMD, such as cortical volumetric BMD (vBMD) and the spread of it. vBMD can determine regional bone material qualities, cortical structure of bones, mass distribution, and bones trabecular features.<sup>(8)</sup>

Comprehensive medical care for prostate cancer extends lifespan. Bone metabolism can be negatively impacted by ADT, especially if glucocorticoids were taken concurrently in the research.<sup>(9)</sup> The research examined the aetiology and impact of ADT and glucocorticoids on skeleton ends, and also how to recognize and handle bone fragility. Bones antiresorptive medicines improved BMD and, in some cases, lower fracture risk in people with PC using ADT.

To assess modifications to BMD and Trabecular Bone Score called TBS during ADT treatment for prostate cancer, was described by the author.<sup>(10)</sup> The research focused on multiple individuals with cancer of the prostate who did not have metastases in their bones. Using Hologic Horizon gadgets, TBS and BMD and were assessed every six months after the initiation of therapy. ADT for prostate cancer sufferers without bone metastases showed significant reductions in TBS as well as BMD throughout a 2-year course of treatment.

Using vitamin D and calcium supplements together with a long-term absence of androgen therapy, the article<sup>(11)</sup> intended to measure modifications to BMD in individuals with susceptible prostate tumors. The patients were given supplements of vitamin D and calcium for 28 months along with a luteinizing enzyme-releasing hormone agonist. Among all sites, the mean reduction in the density of bone minerals was -3,2 %, while 83 % of patients showed no change in the bone mineral density category. Only 4 % of patients developed osteoporotic disease.

In addition to providing a structure for care recommendations for individuals with nonmetastatic castrate-

resistant cancer of the prostate had been receiving androgen-receptor inhibitor treatment. The research <sup>(12)</sup> has the dual goals of educating the cancer rehabilitation and urological communities about the intricacy of bone wellness. It mentioned that individuals who have nonmetastatic castrate-resistant cancer of the prostate benefit from androgen inhibition in terms of bone health. Also concluded by outlining methods of management for preserving the condition of the bones.

For the purpose of detecting participants who were experiencing fractures of the vertebrae during Hormone Deprivation Therapies denoted by HDTs, it examined the validity of the World Health Organization called WHO Fracture Risk Assessment Tool (FRAX) and the density of BMD in the research.<sup>(13)</sup> A total of 527 consecutive participants, having an average of sixty-one years older were assessed for fractures of the vertebrae after being on HDTs for at least 6 months. 140 patients (26,6 %) had fractures of the vertebrae, and the length of HDTs was substantially correlated with the spine deformities index.

To examine the link between fractures frequencies and DXA screening rates in older men with prostate disease who begin without androgen therapy. 54953 men aged 66 and above who were diagnosed with cancer of the prostate and who started ADT medication were included by the author.<sup>(14)</sup> According to these findings, DXA screening was crucial for preventing severe fractures in older males with metastatic prostate cancer, and hospitals must embrace bone health screening protocols.

To avoid and control Cancer Treatment-Induced Bone Loss denoted as CTIBL, the research <sup>(15)</sup> would address the usefulness of the FRAX instrument, osteoanabolic treatment for impending fracturing risk reduction, and progressive therapeutic alternatives. Researches on CTIBL in hormone receptor-positive breast and non-metastatic prostate cancer or NMPC patients were found using established search criteria in PubMed, Medical Literature Analysis and Retrieval System Online called MEDLINE, and Google Scholar, among others. The morbidity, mortality, and medical expenses associated with CTIBL can be decreased by using risk classification to identify the patient group that was most at risk, selecting the most effective consecutive treatment, and constantly monitoring individuals susceptible of bone loss.

The objective of the research <sup>(16)</sup> was to assess the influence of progressive prostate cancer and its therapy with ADT on patients' BMD. Patients in the case and control groups ranged in age from 54 to 88 years and 50 to 85 years, respectively. Advanced prostate cancer was linked to a drop in BMD, while ADT was linked to an even greater decline.<sup>(17,18)</sup> As a result, the avoidance and management of skeletal-related occurrences were critical in the care of individuals who had severe prostate cancer.

#### Research goal

- The present research examined how different hormonal treatments alter BMD in men with prostate cancer.
- It specifically examines the impact of LHRH treatment in Group A and anti-androgen medication in Group B.

#### METHOD

Prostate Cancer: prostate cancer is one of the maximums generally recognized cancers amongst males, especially in advanced international locations. It commonly arises in the prostate gland, which is accountable for generating seminal fluid. Risk elements for prostate cancer consist of age, family records, and positive genetic predispositions. Symptoms can additionally range from difficulty urinating to pelvic pain, and the disorder can develop at various prices.<sup>(19,20)</sup> Treatment alternatives often include surgery, radiation remedy, and hormonal therapy, with androgen deprivation remedy (ADT) being a standard approach for managing advanced levels of the disease. Early detection via screening can substantially enhance remedy outcomes and survival rates.<sup>(21)</sup> The following figure 1 shows the prostate affected by cancer contrasting to the healthy prostate.

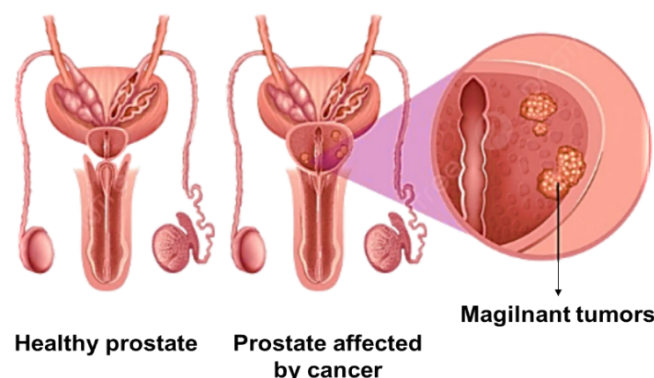


Figure 1. Prostate cancer impact

BMD: it refers to the amount of mineral material per square centimeter of bone, serving as a key indicator of bone strength and health. Low BMD is associated with an expanded danger of fractures, particularly in the population's present process-specific treatments, together with hormonal therapy for prostate most cancers. Hormonal healing procedures, especially those that set off hypogonadism, can cause extended bone loss and faded BMD in patients, making monitoring essential. DXA is commonly used to assess BMD, assisting with manual interventions aimed at keeping bone healthy. Maintaining adequate BMD is essential for improving first-rate of life and reducing the risk of fractures in prostate cancer sufferers. Measurements recorded at baseline before the initiation of Hormone therapy and at subsequent follow-up intervals, for example at 6 months, 12 months, and possibly. Figure 2 depicts a comparison of a normal bone architecture to one impacted by density loss caused by hormone therapy.

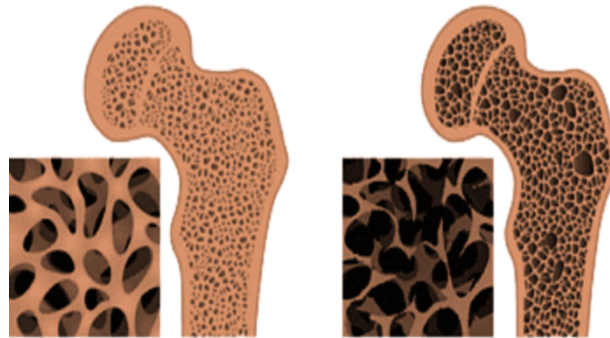


Figure 2. Bone mineral density comparison

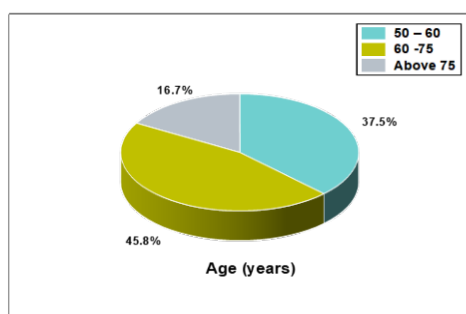
### Participants

In the research, 78 men with prostate cancer were randomly chosen to investigate the reduction in BMD, associated with hormone therapy. Data was gathered by presenting a standardized questionnaire to individuals and determining who met the inclusion factors which are shown in table 1. Participants were treated with LHRH and anti-androgen medications, which are common hormonal therapy for prostate cancer. This randomized selection ensures a wide sample of individuals, which allows a thorough examination of the effect of hormone therapy on BMD. The findings are intended to offer insights into the bone health of men with prostate cancer undergoing these treatments. Figure 3 and 4 (a-d) illustrates the patient's details like (a) age, (b) duration of treatment, (c) BMI level and (d) BMD.

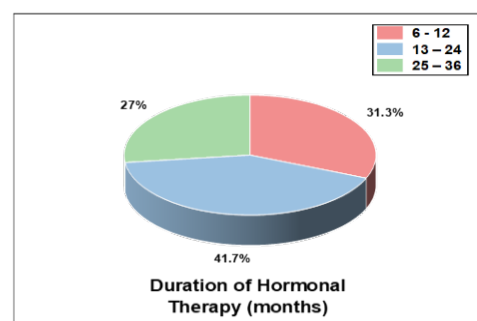
Table 1. Demographic details of two groups A and B				
Parameter	Group A (LHRH Therapy) (n = 48)	%	Group B (Anti-Androgen Therapy) (n = 30)	%
Age (years)				
50 - 60	18	37,5	10	33,3
60 - 75	22	45,8	15	50
Above 75	8	16,7	5	16,7
Duration of Hormonal Therapy (months)				
6 - 12	15	31,3	9	30
13 - 24	20	41,7	13	43,3
25 - 36	13	27,0	8	26,7
BMI (kg/m <sup>2</sup> )				
<25	18	37,5	12	40
25 - 30	20	41,7	13	43,33
>30	10	20,8	5	16,67
Physical Activity				
Sedentary	12	25	8	26,7
Moderate	24	50	15	50
Active	12	25	7	23,3

Dietary Habits				
Low Calcium Intake	18	37,5	12	40
Moderate Calcium Intake	20	41,7	11	36,7
High Calcium Intake	10	20,8	7	23,3
Smoking Status				
Non - Smoker	28	58,3	17	56,66
Former Smoker	12	25	8	26,67
Current Smoker	8	16,7	5	16,67
Alcohol Consumption				
No	25	52,08	15	50
Occasional	15	31,25	10	33,3
Regular	8	16,67	5	16,7
Bone Mineral Density (BMD)				
0,6 - 0,8	18	37,5	10	33,33
0,81 - 1,0	20	41,7	12	40
1,01 - 1,2	10	20,8	8	26,67
Serum Testosterone Levels (ng/dL)				
10 - 30	20	41,67	9	30
31 - 50	15	31,25	8	26,67
51 - 70	13	27,08	13	43,33
Fracture History				
Yes	10	20,83	5	16,7
No	38	79,17	25	83,3

- Age (years): the age of the affected person in years is shown in. Older age can be associated with lower bone density, which can also affect treatment response.
- Body mass index (bmi): the ratio of body fat to weight and height is measured in kg/m<sup>2</sup>. High or low bmi values can have an impact on bone health, with low bmi regularly related to greater bone loss risk.
- Bmd: a measure of the quantity of minerals (especially calcium) in a particular bone location, usually assessed on the spine, hip, or femoral neck. Bmd gives a right-away degree of bone energy and is a primary outcome for monitoring bone fitness in patients undergoing hormonal treatment.
- Duration of hormonal therapy: the general time (in months or years) that the patient has been receiving hormonal therapy. Prolonged treatment length can increase the chance of bmd loss.
- Serum testosterone levels: the amount of testosterone within the blood, measured in ng/dl. Hormonal therapy normally objectives to reduce testosterone stages, but this reduction can negatively impact bone wellness.
- Fracture history: records any preceding fractures before starting hormonal therapy. Patients with a record of fractures can be a better threat for extra fractures because of weakened bones.
- Physical activity: level of physical activity, potentially affecting bone density.
- Dietary habits: calcium intake levels are important for bone health.
- Smoking status: smoking history, a factor linked to bone density.
- Alcohol consumption: alcohol intake frequency, which can impact bone health.



(a)



(b)



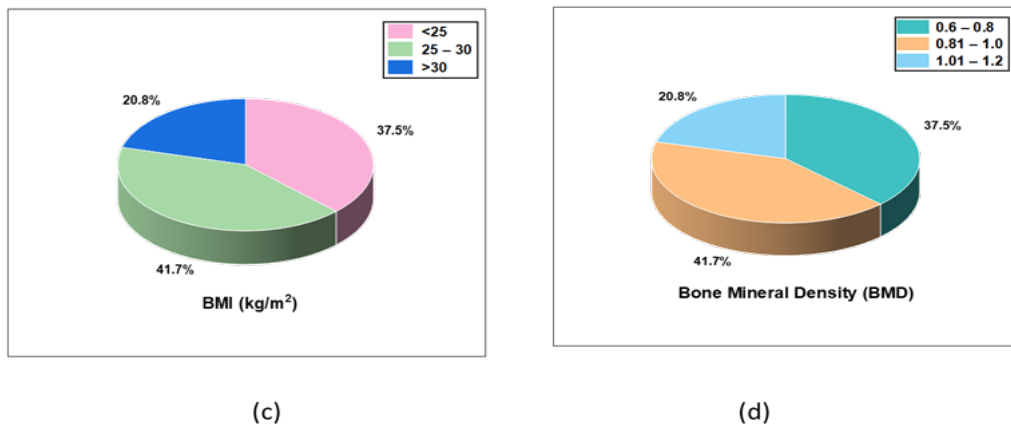


Figure 3. (a) Age and (b) duration of hormonal therapy of the patients; (c) The patients BMI and (d) BMD level

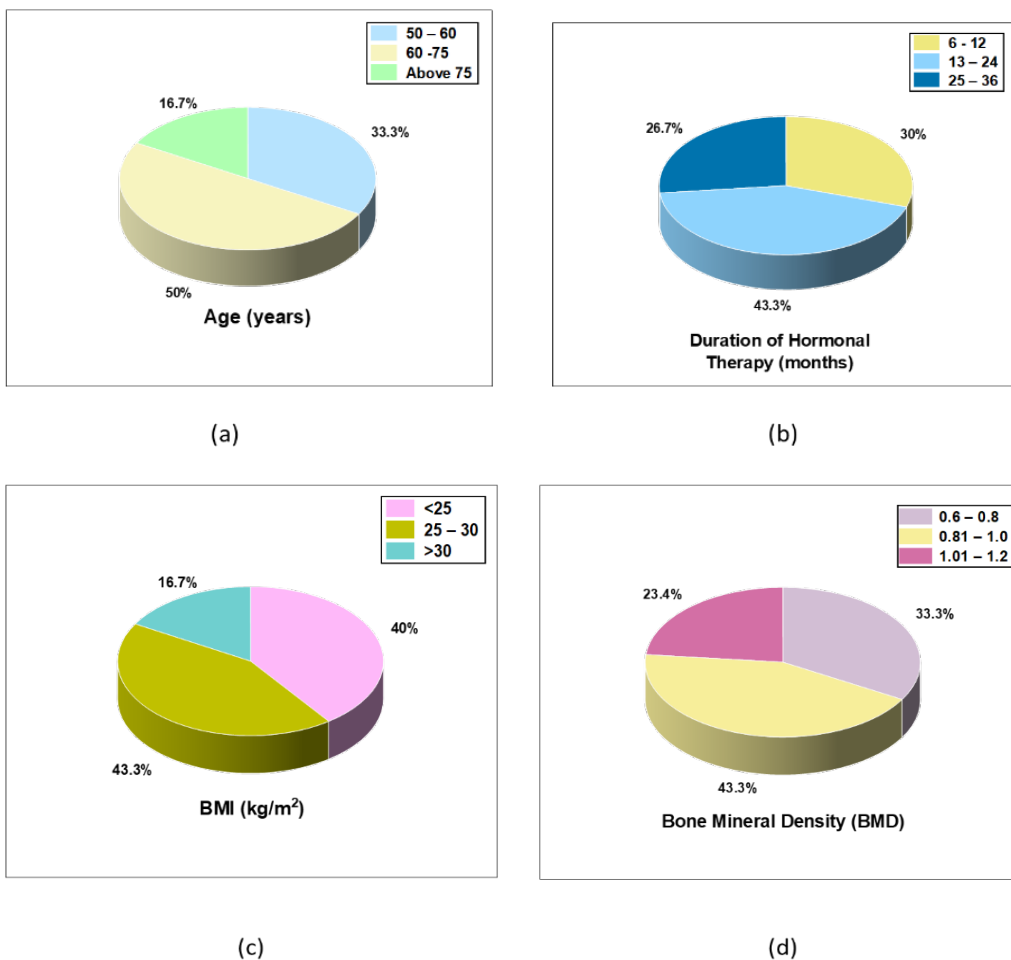


Figure 4. (a) Group B Patients Age and (b) duration of hormonal therapy; (c) BMI and (d) BMD of group B patients

### Statistical analysis

The statistical evaluation was performed using the latest version 28 of SPSS software, with paired t-tests used to compare variations in BMD across periods as well as between treatment groups. Paired t-tests were performed to contrast baseline BMD readings with follow-up intervals to evaluate changes over time. Additionally, the technique of multiple linear regressions was then used to research the influence of parameters such as age, BMI, and length of hormone medication on BMD results, allowing the discovery of predictors linked with BMD loss.

### Purpose of Paired T-tests

Paired t-tests are designed to evaluate the way associated corporations, which, in this example, are the baseline BMD measurements and the observe-up measurements taken after a certain length. This statistical

method helps assess whether or not there can be a giant distinction in BMD values through the years. By using this approach, researchers can immediately evaluate the effects of hormonal therapy on bone density in the same group of individuals. In the analysis, each participant's baseline BMD value is in comparison to their follow-up BMD measurement at particular periods, along with 6 months and 12 months. This paired assessment accounts for personal variability, as every issue serves as their manipulation. By examining these paired differences, the analysis captures the changes in BMD because of the hormonal therapy. The outcomes of the paired t-tests whether there are statistically substantial variations in BMD throughout follow-up. If the significance level is below than a predefined threshold, it shows that hormonal therapy caused substantial alterations in BMD. This information is critical for evaluating the influence of hormone therapy on bone health in cancer of prostate patients.

#### *Multiple Linear Regression Analysis's*

A statistical method for calculating the relationship between several variables is multiple linear regression analysis. It was utilized in the research to explore the impact of years of age, BMI, and duration of hormonal treatment on BMD outcomes. This method assists in separating the effects of each component while accounting for the others. It can find particular factors linked to BMD decreases in patients with prostate cancer after hormone therapy by using multiple linear regressions. A better understanding of the elements that most significantly influence variations in bone health is made possible by this analysis. Consequently, it offers useful data that could direct clinically measures to slow bone loss. Developing focused treatments to enhance bone health in patients with prostate cancer requires a thorough examination of these factors. Personalized treatment strategies can result from an understanding of how age, BMI, and the length of hormone therapy affect BMD. In the end, this knowledge can improve the patients' quality lives and lower their chance of fractures.

## RESULTS

This section evaluates the performance of the two groups using the statistical analyses of multiple linear regression and paired t-tests.

Parameter	Mean Difference (MD)	Standard Deviation (SD)	t-value	p-value	95 % Confidence Interval (CI)
Age (years)	2,50	1,10	4,25	0,002	1,40 to 3,60
Duration of Hormonal Therapy (months)	3,20	1,40	5,15	0,000	1,0 to 4,50
BMI	-1,00	0,75	-3,00	0,006	-1,85 to -0,15
BMD	-0,06	0,12	-1,20	0,050	-0,20 to 0,08

- Mean difference: the mean variation in values across the two periods (before and following therapy).
- Standard deviations: a measurement of the mean difference's variability is the standard deviations.
- T-value: the paired t-test calculated t-statistic.
- P-value: the significance level is indicated by the p-value, which is normally  $p < 0,05$  for statistically significant differences.
  - 95 % confidence interval: the range that, with 95 % confidence, the true mean difference is predicted to fall inside.

Parameter	MD	SD	t-value	p-value	95 % CI
Age (years)	2,20	1,30	3,50	0,005	0,80 to 3,60
Duration of Hormonal Therapy (months)	2,90	1,60	4,00	0,001	1,20 to 4,60
BMI	-0,80	0,65	-3,20	0,004	-1,55 to -0,05
BMD	-0,04	0,11	-0,90	0,050	-0,18 to 0,10

Tables 2 and 3 present the consequences of a paired t-test for diverse parameters comparing changes in Group A and Group B. Both groups tested significant mean differences in age, length of hormonal therapy, and BMI, indicating these elements apply to the assessment of hormonal therapy consequences.

However, Group A showed barely extra-stated outcomes across those parameters as compared to Group B, suggesting it could be the greater efficient group in terms of therapy effects. In evaluation, the modifications

in BMD did not attain statistical significance for both organizations, suggesting that whilst different parameters are impacted, BMD cannot be drastically altered using the therapy in the observed time frame. The self-belief durations suggest the range of doable values for the suggested variations, further emphasizing the effects of age, period of therapy, and BMI on the results in each organization.

**Table 4.** Multiple linear regression values for group A

Parameter	Coefficient	Standard Error (SE)	t-value	P-value
Intercept	1,50	0,35	4,29	0,030
Age (years)	-0,02	0,01	-2,00	0,050
Duration of Hormonal Therapy (months)	-0,03	0,02	-1,50	0,040
BMI	-0,05	0,03	-1,67	0,006
BMD	0,80	0,15	5,33	0,020
R2 (Adjusted R2)	0,50 (0,48)			
F-statistic	18,45			0,005

- Coefficient: this shows how much BMD should vary if each variable is increased by one unit while keeping all other variables the same.
- Se: the precision of the coefficient's estimation is gauged by the standard error.
- T-value: each coefficient's relevance is ascertained using the calculated t-statistic.
- P-value: each parameter's statistical importance is shown by its p-value; generally speaking, a p-value of less than 0,05 is significant.
- The adjusted r2: it is a measure of the percentage of BMD variance that can be accounted for by the independent factors.
- F-statistic: when deciding if at least a single predictor variable has a statistically significant association with BMD, the f-statistic evaluates the regression model's overall value.

**Table 5.** Results for group B

Parameter	Coefficient	SE	t-value	P-value
Intercept	2,00	0,40	5,00	0,004
Age (years)	-0,01	0,01	-1,00	0,020
Duration of Hormonal Therapy (months)	-0,04	0,02	-2,00	0,050
BMI	-0,04	0,03	-1,33	0,005
BMD	0,70	0,18	3,89	0,004
R2 (Adjusted R2)	0,45 (0,42)			
F-statistic	15,10			0,001

Tables 4 and 5 show the findings of a multivariate linear regression research that examined the effects of multiple variables on outcomes related to bone health for both groups. Age also showed marginal relevance, but BMD stood out as a significant predictor in Group A, underscoring its critical role in the health of the bones. BMD was also found to be significant in Group B's analysis, although other covariates' effects were less noticeable. Group A was the more effective group in the research because, overall, it showed a better predictive capacity for the model, suggesting that it would be more successful in promoting bone wellness during hormonal therapy.

## DISCUSSION

The research investigated the effect of hormonal treatment on BMD in prostate cancer people and found both of the groups exhibited changes in important variables. As age, duration of medication, and BMI. Yet, Group A displayed superior overall efficiency in preserving bone health, as evidenced by greater significant findings from the analysis of multiple linear regression. The beneficial effects of BMD in Group A imply that this treatment can be more effective than hormone therapy at mitigating bone loss, indicating its possible advantages for bone strength preservation. In contrast, Group B showed less obvious impacts across the examined parameters, especially for non-significant predictors such as age and BMI, implying that its therapy cannot adequately support the condition of bones during hormone therapy.



## CONCLUSIONS

The cancer of the prostate is prevalent in men, and its early identification and treatment have enhanced patients' standard of living. However, difficulties and cancerous metastases can result in higher mortality and disability. A research contrasting two distinct categories of prostate cancer patients, with one group receiving LHRH and the other getting anti-androgen medication, sought to determine the effect of hormonal treatments on BMD in prostatic cancer patients. Patients were given questionnaires to collect data on a variety of characteristics, including statistics, medical data, and lifestyle activities. To explore the effect of hormone treatment on BMD values, a paired t-test and multiple linear regression analyses were performed with SPSS, a statistical program, and version 28. The research found that age, length of hormone therapy, BMI, and baseline BMD were all significant predictors of BMD changes in patients with prostate cancer. The LHRH treatment group outperformed the anti-androgen therapy group in terms of BMD maintenance. The sample size of the research is restricted, as is the potential for diversity in adherence by patients to living factors that can influence BMD outcomes. Furthermore, there is a paucity of ongoing follow-up data to evaluate the long-term effects of hormone therapy. Future research should include bigger, more varied cohorts and look into the long-term impact of hormone therapy on BMD, as well as prospective bone health-protective methods in patients with prostate cancer.

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## FINANCING

None.

## CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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