Urology

Comparison of Metabolic and Cardiovascular Impact between Gonadotropin-Releasing Hormone Agonists and Orchidectomy for Androgen Deprivation Therapy in Metastatic Carcinoma Prostate

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Abstract	Original Research Article

Background: Metastatic prostate cancer is a global health challenge and requires a balanced approach to preserve the quality of life and extend survival. Current treatment is to offer monotherapy either orchidectomy or GnRH agonists or antagonists to hormone-sensitive metastatic prostate cancer patients. Androgen deprivation therapy increases the risk of obesity, diabetes, dyslipidemia and osteoporosis. ***Objectives:*** This study was done to compare the metabolic and cardiovascular impact of GnRH agonist and orchidectomy for androgendeprivation therapy in metastatic carcinoma prostate. ***Methods:*** This Quasi-experimental study was conducted at the Department of Urology, Dhaka Medical College Hospital, Dhaka during the period from July 2019 to December 2020. A total of 28 patients diagnosed with metastatic prostate cancer were included in the study as per inclusion and exclusion criteria. After counselling, patients were allocated to orchidectomy (Group- A) or GnRH agonist (group-B) as per the patient's choice. After undergoing orchidectomy or receiving GnRH agonists, patients were advised to follow up at 1, 3 and 6 months. Two patients were lost to follow-up. ***Result:*** The mean age of patients in group-A was 66.55(range 58-74) years and in group B was67.8 (62-73) years. There was a significant increase in RBS, triglyceride and a decrease in HDL and bone mineral density at 6 months of group B compared to Group-A. After 6 months, 9.09% of patients in group-A compared to 26.6% of patients in group B had RBS above 11.1 mmol/L. In group-A, 45.45% of patients had triglyceride levels>150 mg/dL compared to 80% in group B. HDL level decreased <40 mg/dL in 45.45% of patients in group-A but 60% in group B. Bone mineral density decreased below -2.5 in 9.09% of patients in group- A compared to 46.66% in group B. Mean S.PSA was around 2 ng/ml in both groups during the follow-up period. The cardiovascular and metabolic impact of orchidectomy was less compared to GnRH agonists. ***Conclusion:*** Though both orchidectomy and GnRH agonists have cardiovascular and metabolic impacts in patients undergoing androgen deprivation therapy for metastatic carcinoma prostate, orchidectomy appears to have a comparatively lesser adverse effect on patient health in these aspects.
Keywords: Metabolic, Cardiovascular, Impact, Gonadotropin-Releasing Hormone Agonists, Orchidectomy.

INTRODUCTION

Prostate cancer is a significant global health challenge, ranking as the second most commonly diagnosed cancer and the sixth leading cause of cancer death among men worldwide. The incidence and mortality rates are expected to rise in the coming years, with an estimated 2.3 million new cases and 740,000 deaths projected by 2040 due to population growth and ageing [1]. In 2020, prostate cancer accounted for 7.3% of new cancer cases and 3.8% of cancer-related deaths globally, with 1,414,259 new cases and 375,304 deaths reported. Bone metastasis is a common occurrence in advanced prostate cancer, with approximately 10% of newly diagnosed patients already having metastases, which increases to 80% in advanced stages. These metastases are associated with poor prognosis, bone pain, and an incurable state in most cases [2].

Prostate cancer cells exhibit a particular affinity for bone, leading to their invasion and proliferation in the axial skeleton, including the spine, pelvis, and ribs [3]. Understanding the global burden of prostate cancer and the propensity for bone metastasis highlights the urgent need for effective management and treatment strategies, focusing on both localized and advanced stages of the disease. Early detection, targeted therapies, and comprehensive care approaches can improve outcomes and quality of life for prostate cancer patients.

Metastatic prostate cancer presents a global health challenge, and the management of this disease remains complex. Orchidectomy, discovered by Charles Huggins [4], was the primary treatment for almost four decades. Hormone-sensitive prostate cancer is typically treated with androgen deprivation therapy (ADT) using LHRH agonists or antagonists or surgical castration. However, emerging evidence suggests that ADT is associated with adverse effects, including cardiovascular events and metabolic changes. ADT leads to increased body mass index, total cholesterol, HDL, LDL, TG, and HbA1C levels, as well as decreased insulin sensitivity [5]. It also results in decreased bone mineral density, putting patients at risk for osteoporosis [6]. However, there is a lack of studies comparing the adverse effects of different ADT modalities.

In our country, the detection of metastatic prostate cancer is rising due to improved diagnostic facilities. Treatment options commonly chosen by patients are orchidectomy or GnRH agonists, but a comparative analysis of their cardiovascular and metabolic impacts is lacking. Therefore, the objective of this study is to assess and compare the cardiovascular and metabolic effects of ADT between orchidectomy and GnRH agonists. Such research is essential to determine the safest and most effective ADT modality for the benefit of our patients.

OBJECTIVES
To compare the metabolic and cardiovascular adverse effects of bilateral orchidectomy with that of GnRH agonist in the treatment of metastatic prostate cancer.

Specific Objective:
- Measurement of BMI, Fasting lipid profile (Total cholesterol, HDL, LDL & TG) before and after ADT to assess cardiovascular impact.
- Measurement of Random blood sugar, HbA1C & Bone mineral density before and after ADT to assess metabolic impact.
- Measurement of serum PSA before and after ADT.

MATERIALS AND METHODS

This quasi-experimental study was conducted in the outpatient and inpatient departments of the Urology Department of DMCH from June 2019 to December 2020. The study included patients who had previously undergone a core biopsy of the prostate, confirming Adenocarcinoma of the prostate. Two groups were formed: Group A consisted of patients who underwent bilateral orchidectomy, while Group B comprised patients who received GnRH agonist therapy. Tc-99 MDP bone scans were performed, revealing up to three hotspots in each patient. The patients were evaluated based on their medical history, physical examination, and previous investigations. Inclusion criteria included being diagnosed with metastatic hormone-sensitive prostate cancer within 12 months before enrollment, while exclusion criteria encompassed non-adenocarcinoma of the prostate, prior ADT or chemotherapy, high-volume disease, incontinence or paraplegia due to vertebral metastasis, or a diagnosis exceeding 12 months from enrollment. After counselling on the available modalities of primary ADT, the patients chose either bilateral orchidectomy or GnRH agonist therapy using Inj. Zoldex (Goserelin) 10.8 mg subcutaneously every 3 months. Follow-up assessments were conducted at 1st, 3rd, and 6th months after the chosen treatment modality.

Data Collection:
Relevant data was collected in a predesigned data collection form and was analyzed with a standard statistical method. No patient was included whose ability to give voluntary consent was questionable. No potential risks existed in designing this study.

Statistical Analysis:
Data was processed and analyzed with the help of computer software SPSS (Statistical Package for Social Science), version 23. The appropriate test statistics were used to analyze the data. The data presented on continuous scale was expressed as mean and standard deviation (SD) from the mean and was compared between groups of interest with the help of student's t-Test, paired & unpaired t-Test was done. Level of significance for all comparative analyses was set at 0.05 and $p<0.05$ were considered significant.

Ethical Consideration
This protocol was approved by the Research Review Committee of the Department of Urology, Dhaka Medical College Hospital. Ethical clearance for the study was taken from the Ethical Review Committee of DMCH. The aims and objectives of the study along with its procedure, risks and benefits of this study were explained to the study subjects in an easily understandable local language. Written informed consent was taken from all the study subjects without exploiting any of their weakness. All the study subjects were assured of adequate treatment for any complications that developed during the study. All the study subjects were assured about their confidentiality

and had the freedom to withdraw themselves from the study at any time.

RESULTS

A total of 28 patients who were diagnosed with metastatic adenocarcinoma of the prostate were enrolled according to inclusion and exclusion criteria. The patients were non-randomly allocated into two groups, group-A and A (bilateral orchidectomy) which had 12 patients and Group B (Inj. Zoladex 10.8mg 3 monthly)

which had 16 patients. One patient from the orchidectomy group and 1 patient from the GnRH agonist group were lost to follow-up. The outcome variables were Body mass index, ,Lipid profile, for assessment of cardiovascular impact and Random blood sugar, HbA1C and Bone mineral density for assessment of metabolic impact. After the measurement of variables for 6 months, they were compared. The findings derived from data analysis are presented below.

Table 1: Distribution of the study subjects according to age (N=26)

Age (years)	Group A (n=11)	Group B (n=15)	*P*-value
<70	7 (63.6)	9 (60.0)	
≥70	4 (36.4)	6 (40.0)	0.926
Mean ± SD	66.55 ± 7.66	67.80 ± 5.49	

Note: Unpaired t-test was done to measure the level of significance. A p-value <0.05 was considered

significant. Group A was the orchidectomy group, and Group B was the GnRH agonist group.
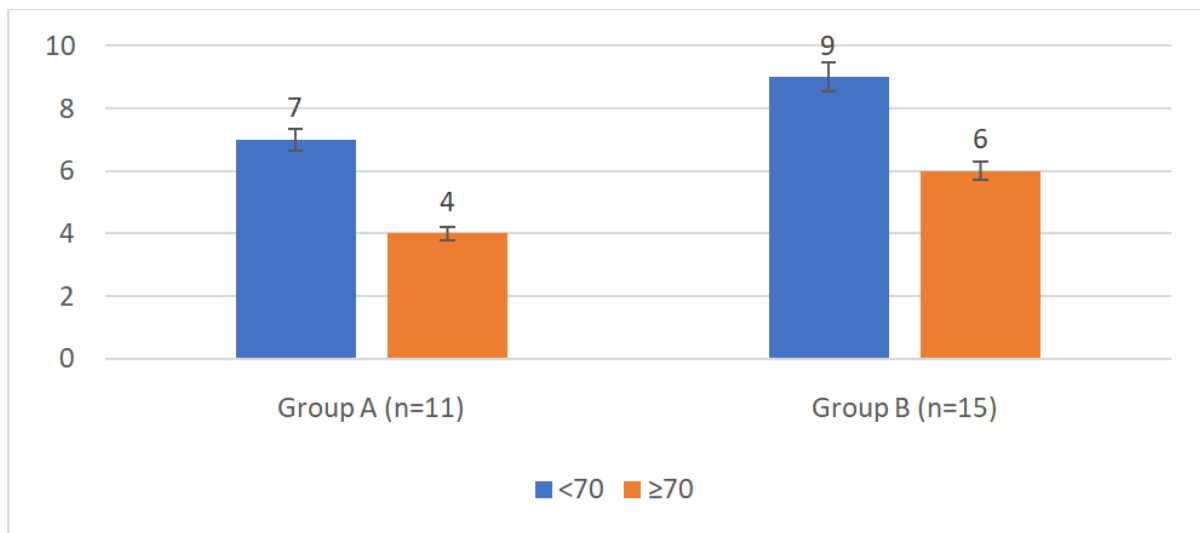

Figure 1: Age distribution

The mean age of the orchidectomy group was 66.55(±7.66) years and that of the GnRH agonist group was 67.80(± 5.49) years. Of the orchidectomy group, 63.6% of patients were below 70 years and 36.4% were above 70 years. In the GnRH agonist group, 60% of

patients were below 70 years and 40% were above 70 years. The difference in mean age between the two groups was not statistically significant (p=0.92) (Table 1).

Table 2: Comparison of variables before ADT (N=26)

Variables	Before orchidectomy (n=11)	Prior to GnRH agonist (n=15)	*P*-value
RBS (mmol/L)	8.54± 4.52	8.67± 4.51	0.943
HbA1C (%)	5.94±1.56	6.03±1.22	0.870
PSA (ng/ml)	19.48±4.70	23.22±7.51	0.302
TC (mg/dl)	162.36±18.40	160.13±26.86	0.815
HDL (mg/dl)	43.00±4.86	40.53±4.49	0.193
LDL (mg/dl)	111.55±16.48	108.53±23.38	0.718
TG (mg/dl)	146.82±40.28	132.87±27.86	0.306
BMD(Lumbar)	-1.63±0.90	-0.78±2.26	0.353
BMD (Femoral)	-1.61±0.60	-1.85±0.99	0.487

Difference of variables between orchidectomy and GnRH agonists before ADT was compared. There

was mean difference of 0.13(±0.01) mmol/L in RBS, 0.09(±0.34) % in HbA1C, 3.74(±2.81) ng/ml in PSA

which was not significant. Regarding lipid profile, the mean difference between total cholesterol (Tc) was 2.23 (±8.46) mg/dl, HDL was 2.47 (±0.37) mg/dl, LDL was 3.02(±6.9) mg/dl & triglyceride (TG) was 13.95 (±12.42) mg/dl. These were not significant. Comparing the difference in bone mineral density showed a mean difference of -0.85(±1.36) in lumbar & -0.24(±0.39) in femoral region which was not significant (Table 2).

Table 3: Lab parameters of the study subjects at different follow-ups(N=26)

Lab parameter	Follow up	Orchidectomy (n=11) (Mean ± SD)	GnRH agonists (n=15) (Mean ± SD)	*P*-value
RBS (mmol/L)	Pre-ADT	8.54 ± 4.52	8.67 ± 4.51	[a]0.943
	At 1st month	8.56±3.75	8.43±4.7	[a]0.783
	At 3rd month	8.40 ± 2.83	8.83 ± 2.55	[a]0.686
	At 6th month	8.52 ± 2.03	10.14 ± 1.89	a0.048
		[b]0.993	[b]0.174	
HbA1c (%)	Pre-ADT	5.94 ± 1.56	6.03 ± 1.22	[a]0.870
	At 1st month	5.87±1.34	6.04±1.25	[a]0.364
	At 3rd month	5.85 ± 1.16	6.07 ± 1.14	[a]0.645
	At 6th month	5.99 ± 1.11	6.13 ± 1.08	[a]0.746
		[b]0.809	[b]0.524	
PSA (b/min)	Pre-ADT	19.48 ± 4.70	23.22 ± 7.51	[a]0.302
	At 1st month	2.08±0.73	2.28±0.49	[a]0.631
	At 3rd month	2.11 ± 0.74	2.21 ± 0.44	[a]0.658
	At 6th month	2.03 ± 0.54	2.14 ± 0.37	[a]0.589
		[b]<0.001	[b]<0.001	

aUnpaired t-test bPaired t-test was done, and p-value <0.05 was considered significant.

The difference between orchidectomy & GnRH agonist receivers in random blood sugar was 0.13(±0.01), 0.13(±0.95) and 0.43(±0.28) before ADT, 1st and 3rd month respectively, which was not significant. In the 6th month, there was a difference of 1.62(±0.14) between the two groups, which was statistically significant. Here 9.09% of patients showed RBS> 11.1 mmol/L, compared to 26.6% patients of in group B (Table 3).

Table 4: Lipid profile of the study subjects at different follow-ups (N=26)

Lipid profiles	Follow-ups	Orchidectomy (n=11) (Mean ± SD)	GnRH agonist (n=15) (Mean ± SD)	*P*-value
TC (mg/dl)	Pre- ADT	162.36 ± 18.40	160.13 ± 26.86	[a]0.815
	At 1st month	164±19.34	162±25.46	[a]0.439
	At 3rd month	168.00 ± 17.41	166.80 ± 26.54	[a]0.897
	At 6th month	176.09 ± 22.07	175.80 ± 28.39	[a]0.978
		[b]0.002	[b]<0.001	
HDL (mg/dl)	Pre- ADT	43.00 ± 4.86	40.53 ± 4.49	[a]0.193
	At 1st month	42.78±4.23	40.40±4.34	[a]0.665
	At 3rd month	40.82 ± 3.74	39.13 ± 5.00	[a]0.357
	At 6th month	41.00 ± 3.66	36.93 ± 4.35	a0.019
		[b]0.151	[b]<0.001	
LDL (mg/dl)	Pre- ADT	111.55 ± 16.48	108.53 ± 23.38	[a]0.718
	At 1st month	111.56±16.34	110.23±23.31	[a]0.635
	At 3rd month	117.00 ± 16.17	114.73 ± 24.53	[a]0.792
	At 6th month	123.27 ± 15.72	119.93 ± 29.40	[a]0.736
		[b]<0.001	[b]<0.001	
TG (mg/dl)	Pre- ADT	146.82 ± 40.28	132.87 ± 27.86	[a]0.306
	At 1st month	147.21±39.78	135.33±25.78	[a]0.568
	At 3rd month	152.09 ± 38.66	142.27 ± 31.58	[a]0.446
	At 6th month	149.81 ± 16.26	164.80 ± 17.70	**a0.037**
		[b]0.711	[b]<0.001	

aUnpaired t-test bPaired t-test was done, and p-value <0.05 was considered significant. Group A is orchidectomy & Group-B is GnRH agonist receiver.

In the lipid profile, the difference between the two groups showed, in total cholesterol the difference was 2.23(±8.46), 2.0(±5.82), 1.2(±9.13) and 0.29(±6.32) respectively, which was not significant.

The HDL count between the two groups showed a difference of 2.47(±0.37) in baseline, 2.38(±0.11) in 1st and 1.69(±1.26) in 3rd month which was not significant. In the 6thmonth, it showed a difference of 4.07(±0.69) which was statistically significant. In the Orchidectomy group, 45.45% of patients showed low levels of HDL compared to 60% patients of with GnRH agonists. The HDL count between the two groups showed a difference of 2.47(±0.37) in baseline, 2.38(±0.11) in 1st and 1.69(±1.26) in 3rd month which was not significant. In the 6thmonth, it showed a difference of 4.07(±0.69) which was statistically significant. In Orchidectomy group 45.45% patients

showed low level of HDL compared to 60% patients of GnRH agonist. The LDL count between the two groups showed difference of 3.02(±6.9), 1.33(±6.97), 2.27(±8.36) and 3.34(±13.68) respectively which was not significant. The triglyceride between the groups showed a difference of 13.95(±12.42) in baseline, 11.88(±14) in 1st and 9.82(±7.08) in 3rd month which was not significant. In 6th month it showed a difference of 14.99(±1.44) which was statistically significant. In the orchidectomy group, 45.45% of patients showed TG level >150 mg/dl, compared to 80% of patients of GnRH agonist (Table 4).

Table 5: Comparison of variables before & after GnRH agonist (n=15)

Variables	Before GnRH agonist n=15	6 months after GnRH agonist n=15	*P*-value
RBS (mmol/L)	8.67± 4.51	10.14±1.89	0.174
HbA1C (%)	6.03±1.22	6.13±1.08	0.524
PSA (ng/ml)	23.22±7.51	2.14±0.37	<0.001
TC (mg/dl)	160.13±26.86	175.80±28.39	<0.001
HDL (mg/dl)	40.53±4.49	36.93±4.35	<0.001
LDL (mg/dl)	108.53±23.38	119.93±29.40	<0.001
TG (mg/dl)	132.87±27.86	164.80±17.70	<0.001
BMD(Lumbar)	-0.78±2.26	-1.48±2.09	<0.001
BMD (Femoral)	-1.85±0.99	-2.44±0.65	<0.001

Paired t-test was done. P-value < 0.05 was considered significant.

The comparison of variables before & after administration of GnRH agonist showed, the mean rise of RBS 1.47±2.62 mmol/L and increased HbA1C 0.1±0.14% after 6 months, but these were statistically not significant. There was a fall in PSA value of 21.08±7.14 ng/ml in 6 months which was significant. Comparison of lipid profile revealed an increase in total cholesterol of 15.67± 1.53 mg/dl, decrease in HDL of 3.6± 0.14 mg/dl, increase in LDL of 11.4±6.02 mg/dl & increase in triglyceride of 31.93± 10.16 mg/dl, all of which were significant. Bone mineral density showed a mean decrease of 0.7± 0.17 in the lumbar & 0.59± 0.3 in the femoral region after 6 months, both of which were significant (Table 5).

DISCUSSION

The management of metastatic hormone-sensitive prostate cancer poses a dilemma for physicians, as balancing disease control with quality of life is challenging. Androgen deprivation therapy (ADT) with LHRH agonists/antagonists or surgical castration is recommended according to the AUA guideline 2020 [7]. However, ADT is associated with metabolic and cardiovascular adverse effects that can harm patients. This quasi-experimental study aimed to compare the metabolic and cardiovascular impact of surgical castration and medical castration (GnRH agonist) in Bangladeshi metastatic prostate cancer patients, using affordable and accessible parameters.

A total of 28 patients diagnosed with metastatic adenocarcinoma of the prostate were enrolled based on inclusion and exclusion criteria. They were

non-randomly allocated into two groups: Group A (bilateral orchidectomy) with 12 patients and Group B (Inj. Zoladex 10.8mg every 3 months) with 16 patients. Two patients, one from each group, were lost to follow-up. Outcome variables included body mass index, lipid profile (for assessing cardiovascular impact), random blood sugar, HbA1C, and bone mineral density (for assessing metabolic impact). These variables were measured and compared over 6 months.

In this study, the age of the patients ranges from 55-80 years. The mean age of the orchidectomy group was 66.55(± 7.66) years and that of the GnRH agonist group was 67.80(± 5.49) years. Age distribution was almost homogenous in both groups. Median age was 65 (IQR 62.5-71.00) years in group-A and 68(IQR 64.00-70.5) years in group B. Age distribution does not support Chen *et al.,* [8] where the median age of the GnRH agonist group was 75(±11.0) years and the orchidectomy group was 76(±10.0) years. Similarly, it does not support Sun *et al.,* [9] where the median age of GnRH agonists was 78(72-83) and orchidectomy 78(73-83). The difference with the present study maybe due to higher life expectancy in Sweden and the American population causing late presentation of the disease.

Comparison of variables before ADT showed a mean difference of 0.13(±0.01) in random blood sugar, 0.09(±0.34) % in HbA1C and 3.74(±2.81) ng/ml in PSA which was not significant. Regarding lipid profile, the mean difference between total cholesterol was 2.23(±8.46) mg/dl, HDL was 2.47(±0.37), LDL was 3.02(±6.9) and TG was 13.95(±12.42) mg/dl. These

differences were not significant (p>0.05). Differences in bone mineral density were -0.85(±1.36) in the lumbar and -0.24(±0.39) in the femoral region which was not significant (p>0.05). These findings signify a homogenous population, which helps in the comparison of outcomes between two groups. It is similar to Tan *et al.,* [10] whose baseline comparison showed no significant difference.

Random blood glucose between the two groups showed no significant difference in the first 3 months. It showed a mean difference of 1.62(±0.14) in 6 months of follow-up, which was statistically significant. The orchidectomy group had 9.09% patients and the GnRH agonist group had 26.6% patients who had RBS >11.1 mmol/L. This is similar to Chen *et al.,* [8] who showed an increased incidence of diabetes which was more in the GnRH agonist group than the orchidectomy group. It also is similar to a study by Keating *et al.,* [11] which shows treatment with GnRH agonists was associated with statistically significantly increased risks of incident diabetes (for GnRH agonist therapy, 159.4 events per 1000 person-years vs. 87.5 events for no androgen deprivation therapy, difference = 71.9).

In a comparison of HbA1c between the bilateral orchidectomy group and GnRH agonist group, there was a mean rise of 0.05(±0.45) % and 0.1(±0.14) % respectively, which was not significant. This is contrary to a study by Mitsuzuka K *et al.,* [12] who found that a 2.7% rise in HbA1C was observed in 1year administration of ADT. This may be due to the short duration of follow-up. PSA has prognostic value in the treatment of carcinoma prostate. In this study, the mean S.PSA in the orchidectomy group was 2.03(±0.54) at the end of 6 months compared to 2.14(±0.37) in the GnRH group. this is different from a similar study [10] which showed that 65.6% of patients in the orchidectomy group and 67.2% of the GnRH agonist group had PSA below 1 ng/ml at the end of 6 months. The cohort size was 523 which may explain the difference in PSA level compared to the current study.

The lipid profile comparison of the two groups showed no significant difference in the first 3 months, but after 6 months, there was a decrease in HDL level and an increase in triglyceride level which was significant. 45.45% of patients in orchidectomy and 60% of patients in the GnRH agonist group had HDL levels below 40mg/dL. Also, 45.4% of patients in the orchidectomy group and 80% of patients in the GnRH agonist group had triglyceride levels above 150 mg/dL. This is similar to the study of Chen D *et al.,* [8], who found that hyperlipidemia was more in the GnRH agonist group than the orchidectomy group. But it is contrary to the study by Mitsuzuka K *et al.,* [12] who showed that there was an annual increase in HDL (7.8%) as well as Triglyceride (16.2%). This difference may be due to the diet and healthy lifestyle of the Japanese population. Also, as the Bengali diet relies heavily on white rice, an increase in triglyceride levels is not unusual.

In comparing bone mineral density, there was no significant difference in lumber region between the two groups. In femoral region, 9.09% patients of orchidectomy and 46.66% patients of GnRH group had osteoporosis at 6 month of follow up, which was significant. This was similar to the study done by Sun *et al.,* (2015) who showed that orchidectomy was associated with a significantly lower risk of any fractures (HR, 0.77; 95% CI, 0.62-0.94). It is also similar to a study by Alibhai *et al.,* [13] who concluded that ADT was associated with significant losses in lumbar spine BMD compared to controls (−2.57 %, p=0.006), with a trend towards greater declines at the total hip (p=0.09). It is also a similar study [10] that showed that at 1-year post-ADT, the incidence of skeletal-related pathological fractures was lower in the orchidectomy group compared to the GnRH group (7.3% vs. 9.3%). Current study only did follow-up for 6 months, so on further follow-up may give us a clearer picture.

Comparison of variables before and after orchidectomy showed a mean increase in total cholesterol 13.73(±3.67) mg/dl and an increase in LDL 11.72(±0.76) mg/dl which were significant (p<0.001). There was a decrease in bone mineral density of -0.57 in the lumbar and -0.37(±0.23) in the femoral region after 6 months which were significant (p<0.001). This is similar to Sharafeldeen who observed a decrease in BMD in both the lumbar and femoral region in the orchidectomy group after 6 months, which was significant [14].

Comparison of variables before and after GnRH administration showed a mean increase in total cholesterol 15.67(±1.53) mg/dl, LDL 11.4(± 6.02) mg/dl, TG 31.93(±10.16) mg/dl and decreased HDL 3.6(±0.14) mg/dl after 6 months, all of which were significant (p<0.001). This is similar to Morote *et al.,* [8] who found there was significant increase in total cholesterol, LDL, HDL and TG after 6 months in patients receiving GnRH agonist. The fall in HDL in the current study, maybe due to a sedentary lifestyle and diet difference with the Turkish population. There was also a significant decrease in bone mineral density of the lumbar 0.7(±0.17) and femoral 0.59 (±0.3) region after 6 months. It is similar to Sharafeldeen who found significant decrease in bone mineral density in both lumbar and femoral region in medical castration group after a follow up of 6 months [14].

CONCLUSION
Both orchidectomy and GnRH agonists cause cardiovascular and metabolic changes which are not favourable for the patient, but orchidectomy has less

harmful cardiovascular and metabolic impact on patient health.

Limitations of Study
- The sample size in each group was relatively small due to the ongoing COVID-19 pandemic. So, the findings in this study may not be generalized on a large scale.
- Short follow-up period. So, the long-term outcome could not be evaluated.
- It was a single-centre study. Variations in outcomes in other hospitals could not be compared.
- Confounding factors were not evaluated like smoking and over-the-counter drug use.

RECOMMENDATIONS

According to the findings of this study, patients undergoing ADT should be routinely evaluated for DM and dyslipidemia as well as annual assessment of bone mineral density. A large, multi-center comparative study with long term follow up is needed for further assessment of the patient's cardiovascular and metabolic safety.

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