



Original Article

Musculoskeletal Changes Over Six Months of Androgen Deprivation Therapy in Men with Prostate Cancer: A Prospective Observational Study

Rodrigo B. Buksman¹, Veronica F. Vianna¹, Erika C. Rodrigues¹, Talita P. Pinto¹, Fabio V. dos Anjos^{1,2}, Arnaldo Couto³, Daibes R. Filho⁴, Daniel Herchenhorn¹, Maria Eugenia L. Duarte¹

¹D'Or Institute for Research and Education (IDOR), Rio de Janeiro, Brazil

²Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil

³State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

⁴São Vicente D'Or Oncology Center, Rio de Janeiro, Brazil

Abstract

Objective: To investigate changes in muscle, bone, and functional parameters over six months of ADT in men with prostate cancer (PCa), with emphasis on sarcopenia. **Methods:** Thirty men with PCa were prospectively evaluated at baseline; 26 completed the 6-month ADT follow-up, and 25 completed all assessments. Body composition, bone mineral density, muscle strength, balance, gait, functional performance, and physical activity were assessed using standardized methods. **Results:** After six months, lean mass decreased by 1.09 kg (95% CI, -1.83 to -0.35; effect size, -0.61), while handgrip strength decreased by 3.62 kgf (95% CI, -5.04 to -2.19; Cohen's d_z = -1.03). Fat mass and body fat percentage also increased significantly at six months. Lumbar spine BMD decreased by 0.033 g/cm² (95% CI, -0.052 to -0.013; effect size, -0.70), while postural sway area increased by 0.011 m²/s⁴ (95% CI, 0.004 to 0.018; Cohen's d_z = 0.62). Mean gait and mobility measures showed no significant changes. Osteosarcopenia occurred in two participants. **Conclusions:** ADT was associated with concurrent changes in muscle, bone, and postural stability parameters at six months. These findings support monitoring of musculoskeletal and functional parameters during treatment and the implementation of appropriate preventive interventions aimed at minimizing osteosarcopenic and functional impairment.

Keywords: Prostate cancer, Androgen deprivation therapy, Osteosarcopenia, Muscle strength, Body composition

Introduction

Prostate cancer (PCa) remains one of the most prevalent malignancies among men worldwide and represents a major cause of cancer-related morbidity and mortality, particularly in aging populations. Its global burden is expected to increase further over the next decades due to population aging, broader access to diagnostic strategies, and improved survival associated with contemporary systemic therapies¹⁻⁴.

Androgen deprivation therapy (ADT) constitutes the biological cornerstone of treatment for advanced and metastatic PCa because tumor growth is strongly dependent on androgen receptor signaling^{5,6}. Over recent years, treatment paradigms have shifted toward earlier and more intensive androgen blockade, frequently combined

with chemotherapy or second-generation androgen receptor pathway inhibitors, resulting in significant survival gains in advanced disease^{7,8}. However, despite its oncological benefits, ADT is also associated with

The authors have no conflict of interest.

Corresponding author: Dr. Maria Eugenia L. Duarte, D'Or Institute for Research and Education (IDOR), Rua Diniz Cordeiro, 30, Botafogo, Rio de Janeiro, RJ, 22281-100

E-mail: meugenia.int@gmail.com

Edited by: George Lyritis

Accepted 23 September 2026

important systemic adverse effects, particularly involving metabolic dysfunction, cardiovascular complications, and musculoskeletal impairment^{5,9,10}.

The consequences of ADT have become increasingly relevant because most patients with PCa already present age-related declines in muscle and bone health at treatment initiation. Testosterone suppression may accelerate reductions in muscle strength, lean mass, physical performance, and mobility, contributing to greater functional vulnerability, fall risk, and loss of independence^{11,12}. ADT-related muscle function decline may also impair postural stability and mobility, potentially increasing fall risk and functional dependence. Mechanistically, ADT has been associated with anabolic resistance, reduced protein synthesis, increased intramuscular fat infiltration (myosteatosis), and impairment in neuromuscular performance, all contributing to progressive functional decline¹³.

Concurrently, ADT-related hormonal deprivation negatively affects bone remodeling and skeletal integrity. Reduced testosterone and estradiol levels favor osteoclastic activation, accelerated bone resorption, and progressive reduction of bone mineral density and microarchitecture, increasing skeletal fragility and fracture risk^{10,14}. Importantly, accumulating evidence suggests that reduced bone and muscle performance in this setting should not be interpreted as isolated processes, but rather as interconnected manifestations of a shared vulnerability phenotype^{15,16}.

Osteosarcopenic phenotypes have increasingly been recognized in older adults with PCa exposed to ADT, reflecting the biological interaction between muscle and bone through shared metabolic and mechanical pathways^{15,16}. Hormonal dysregulation and altered muscle-bone crosstalk involving inflammatory cytokines appear to contribute to the simultaneous functional decline of both tissues¹⁷. Clinically, the coexistence of sarcopenic and osteoporotic alterations has been associated with worse outcomes than either condition alone, including increased risks of falls, fractures, disability, hospitalization, and mortality¹⁸. In the oncological setting, osteosarcopenic changes may represent an important marker of poor functional prognosis, particularly during ADT exposure, when hormonal suppression superimposes on aging-related neuromuscular decline and comorbidities^{19,20}. Nevertheless, important gaps remain regarding the musculoskeletal effects of ADT, especially in studies integrating bone health, sarcopenic alterations, and functional performance within a unified osteosarcopenic framework²¹. Understanding the impact of ADT on the muscle-bone system may therefore be clinically relevant for identifying patients at higher risk of functional decline and for developing preventive and therapeutic strategies focused on preserving mobility, independence, and quality of life. Therefore, the present study aimed to evaluate

changes in muscle-bone and functional parameters over six months of ADT in patients with PCa, with particular emphasis on sarcopenic alterations observed during treatment.

Methods

Study design and participants

This was a prospective longitudinal observational cohort study designed in accordance with STROBE recommendations. Consecutive patients with histologically confirmed prostate adenocarcinoma and clinical indication for ADT were recruited from oncology and urology services within a private healthcare network in Rio de Janeiro, Brazil. Baseline musculoskeletal assessments were scheduled as close as possible to ADT initiation. Eligible patients were enrolled prior to or shortly after ADT treatment initiation and reassessed six months after baseline testing. ADT regimens included pharmacological castration using gonadotropin-releasing hormone (GnRH) or luteinizing hormone-releasing hormone (LHRH) agonists or antagonists, administered alone or in combination with an androgen receptor pathway inhibitor (ARPI), according to individualized clinical indication. Exclusion criteria included previously diagnosed and/or treated osteometabolic disease before study enrolment, neurological or neuromuscular disorders affecting balance or mobility, functional inability to perform physical tests, active non-prostate malignancies, and inability to complete follow-up assessments.

Clinical and demographic data

Baseline characterization included age, body mass index (BMI), height, weight, ethnicity, comorbidities, and relevant time intervals (time from diagnosis to ADT initiation and time from ADT initiation to baseline assessment). Race/skin colour was self-reported by participants. Comorbidities were systematically categorized (cardiometabolic, neuropsychiatric, infectious, and respiratory conditions). Information on concomitant non-oncological medication use, prostate cancer characteristics, treatment-related variables were collected. Treatment regimens were categorized as combined therapy, central ADT monotherapy, or peripheral antiandrogen monotherapy. Combined therapy consisted of central ADT with a GnRH agonist or antagonist plus an ARPI (apalutamide, darolutamide, or enzalutamide). Central ADT monotherapy consisted of a GnRH agonist or antagonist without concomitant ARPI. Peripheral antiandrogen monotherapy consisted of treatment with an antiandrogen without concomitant GnRH agonist or antagonist therapy.

Body composition and bone mineral density assessment

Body composition and bone mineral density (BMD) were assessed using dual-energy X-ray absorptiometry

(DXA) (GE Lunar Prodigy Advance; GE Healthcare, Madison, WI, USA), with enCORE software version 18, following standardized manufacturer positioning and calibration procedures. All scans were performed with participants in the supine position, wearing light clothing and without metallic objects, by a trained technician blinded to clinical outcomes. Whole-body DXA analysis provided measurements of total and regional body composition, including body mass index (BMI, kg/m²), fat mass index (FMI, kg/m²), total fat mass (kg), total lean mass (kg), and body fat percentage (%). Regional adiposity distribution was further quantified in android and gynoid compartments, from which the android/gynoid fat ratio (A/G ratio) was derived. Segmental analysis included trunk, abdominal, upper limb, and lower limb lean and fat mass. Bone mineral density (g/cm²) was measured at clinically relevant skeletal sites, including the lumbar spine (L1–L4), femoral neck, and total proximal femur. Corresponding T-scores were calculated based on manufacturer reference databases. Quality control procedures were performed prior to each acquisition, and all scans were analyzed by the same experienced operator to reduce interobserver variability.

Muscle strength and muscle mass assessment

Muscle strength was assessed by handgrip strength (HGS) using a calibrated Jamar[®] hydraulic dynamometer. Participants were evaluated in the seated position, with shoulders adducted and neutrally rotated, elbow flexed at 90°, forearm supported, and wrist in a neutral position, following standardized assessment procedures. Three maximal voluntary contractions were performed with the dominant hand, with brief recovery intervals between attempts. The highest value obtained across the three trials was used for analysis and expressed in kilograms (kgf). Low muscle strength was defined according to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2)¹¹ criteria as HGS <27 kg. Muscle mass was estimated from whole-body DXA scans through appendicular skeletal muscle mass (ASM), calculated as the sum of lean soft tissue mass from both upper and lower limbs. The Baumgartner Index (BI) or appendicular skeletal muscle mass index (ASMI), was calculated by dividing ASM by height squared (kg/m²), providing an estimate of muscle mass adjusted for body size. This index was used to monitor changes in skeletal muscle mass during ADT exposure and to characterize sarcopenia-related alterations.

Functional tasks and postural balance

Standing balance was assessed over a 30-second period while participants stood barefoot and fixated on a visual target positioned 1 m in front of them at eye level. Three trials were performed, with a 30-second rest interval between trials. Standardized foot positioning was maintained throughout all trials. Functional mobility was evaluated using the Timed Up and Go (TUG) test.

After one familiarization trial, participants completed one timed trial in which they stood up from a chair, walked 3 meters, turned around, returned to the chair, and sat down. Completion time was recorded using a stopwatch. Gait performance was assessed using the 10-Meter Walk Test (10MWT). Participants completed four trials along a 14-m walkway, with the central 10 m used for analysis: two at a self-selected comfortable speed and two at the fastest safe speed. Walking time was recorded using a stopwatch. Gait speed was calculated as distance divided by time (10 m/time in seconds).

Accelerometer data acquisition and processing

Trunk acceleration was recorded during the three 30-second trials of quiet standing and during the four gait trials of the 10MWT, using an accelerometer positioned over the spinous process of the fifth lumbar vertebra (L5)^{22–24} and secured with a hypoallergenic adhesive tape (Hypafix, Leukoplast). Signals were acquired using the Trigno Wireless System (Delsys, USA) and recorded with EMGworks software. Data were sampled at 148 Hz with 16-bit resolution, and an acquisition range of ± 2 g. Data were recorded by two assessors from the same research group, each with 15 years of experience in biomedical data collection and trained in the study protocol. Both were blinded to previous measurements.

Raw acceleration data from both quiet-standing and gait tasks were processed offline using MATLAB (R2024b, MathWorks, USA). The anteroposterior (AP), mediolateral (ML), and vertical acceleration components were extracted for each trial. Each acceleration signal was visually inspected for data quality. To account for sensor tilt and misalignment relative to the body, the three-dimensional acceleration signals were transformed into a true horizontal-vertical Cartesian coordinate system using the mathematical procedure described by Moe-Nilssen²⁵.

For the quiet-standing task, the transformed acceleration signals were low-pass filtered using a fourth-order Butterworth filter with a 3.5-Hz cutoff frequency and zero-phase filtering to attenuate high-frequency noise. Linear trends were removed before analysis²². Postural sway magnitude was quantified using the root mean square (RMS) of the filtered acceleration signals separately for the AP and ML directions. Frequency-domain parameters were derived from the power spectral density estimated using Welch's method, including mean frequency (MF) of the AP and ML acceleration signals. Sway area was calculated as the area of the 95% confidence ellipse derived from the principal components of the AP-ML acceleration data²⁶. Postural balance parameters were averaged across the three quiet-standing trials. For seven participants, one of the three trials was excluded at either the baseline or 6-month assessment because of external disturbances, participant movement, or inability to maintain the required posture; the remaining valid trials

were averaged for analysis.

For the gait task, the walking period of each trial was identified and analyzed separately. Zero-valued samples, considered indicative of signal loss, were replaced with the median value of the corresponding signal before further processing. Following coordinate correction, the vertical trunk acceleration signal was detrended and low-pass filtered using a fourth-order Butterworth filter with a 10-Hz cutoff frequency and zero-phase filtering²⁴. Gait events were identified from the filtered vertical acceleration signal. The signal was first integrated and subsequently differentiated using a Gaussian continuous wavelet transform to facilitate the detection of initial contact (IC) and final contact (FC) events. IC and FC events were identified from peaks in the resulting signals using amplitude thresholds and minimum peak-distance criteria defined relative to the sampling frequency^{23,24}. To minimize the influence of gait initiation and termination, the first three and last three detected steps of each trial were excluded from the analysis. Gait parameters were averaged across valid trials separately for the comfortable and fast walking conditions.

Based on the detected gait events, spatiotemporal parameters were calculated for each walking trial, including cadence, step length, step velocity, and stride time. Step length was estimated using an inverted pendulum model, with vertical displacement of the center of mass derived from double integration of the vertical acceleration signal within each step cycle. A 0.1-Hz high-pass filter was applied to minimize integration drift^{23,27}. Step velocity was calculated as the ratio of step length to step time. Mean values of the spatiotemporal parameters were calculated for each trial and averaged across the two valid trials separately for the comfortable and fast walking conditions.

Physical activity assessment

Habitual physical activity was assessed using the validated Portuguese version of the International Physical Activity Questionnaire (IPAQ), which captures self-reported physical activity performed during the previous seven days across different intensity domains. Activities were classified as walking, moderate-intensity, or vigorous-intensity physical activity according to the IPAQ scoring protocol. Only activities performed continuously for at least 10 minutes were included in the analysis. For each activity category, weekly energy expenditure was estimated by multiplying frequency (days/week), duration (minutes/day), and the corresponding metabolic equivalent of task (MET) value. Total physical activity was calculated as the sum of MET-minutes per week derived from all activity domains and expressed as MET-min/week. This measure was used to characterize overall physical activity level and to monitor changes in habitual activity during the six-month follow-up period of ADT exposure.

Diagnostic criteria

Sarcopenia was defined according to the EWGSOP2 criteria, requiring the coexistence of low muscle strength and reduced muscle mass. Low muscle strength was defined as handgrip strength (HGS) <27 kg, and low muscle mass as a Baumgartner Index/ASMI (appendicular skeletal muscle mass/height²) <7.0 kg/m². Osteosarcopenia was defined as the coexistence of sarcopenia and osteoporosis (T-score ≤ -2.5 SD), according to DXA-derived measurements^{15,18,28}. Functional performance parameters, including gait speed and Timed Up and Go (TUG) test results, were considered complementary indicators of physical function. Falls and fragility fractures were prospectively monitored by self-report throughout follow-up. Fragility fractures were defined as fractures resulting from low-energy trauma, such as a fall from standing height or fractures occurring in the absence of significant trauma.

Statistical Analysis

Analyses were performed using all available paired measurements for each outcome, with outcome-specific denominators reported according to data availability. No imputation was performed for missing data, and no observations were excluded from the analyses based on being statistical outliers. Continuous variables are presented as mean $\pm$ standard deviation (SD), and categorical variables as absolute and relative frequencies. Changes between baseline and the 6-month follow-up were analyzed using paired-samples Student's t-tests when paired differences were normally distributed and Wilcoxon signed-rank tests when the normality assumption was not met. Paired changes are reported as mean differences with 95% confidence intervals (CIs) for outcomes analyzed using paired t-tests and as median differences with 95% CIs for outcomes analyzed using Wilcoxon signed-rank tests. The 95% CIs for median paired differences were estimated using percentile bootstrap resampling with 10,000 resamples. Standardized effect sizes were calculated to complement p-values and quantify the magnitude of within-participant changes. Cohen's *dz* was calculated for paired t-tests, whereas effect size *r* was calculated for Wilcoxon signed-rank tests. Given the exploratory nature of the study and the absence of a prespecified primary outcome, no formal adjustment for multiple comparisons was applied. Therefore, findings across the assessed outcomes were considered exploratory and hypothesis-generating. A sensitivity analysis using the same statistical procedures was performed in participants who completed the 6-month follow-up and were assessed at baseline on the same day as ADT initiation (*n*=17). Statistical analyses were performed using SPSS version 21.0 (IBM Corp., Chicago, IL, USA), and statistical significance was defined as *p*<0.05.

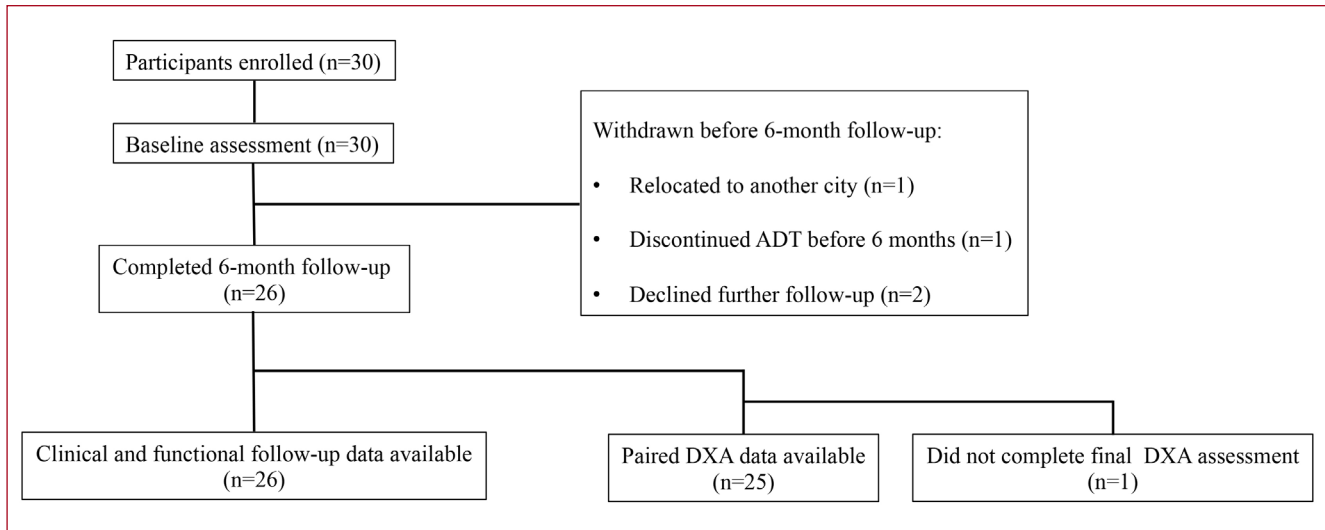


Figure 1. Flow diagram of participant recruitment, follow-up, and availability of outcome data.

Results

Participant flow and baseline characteristics

Between July 2024 and June 2025, 30 patients were consecutively screened and enrolled. Out of the 30 participants enrolled, none underwent assessment prior to beginning ADT treatment. Nineteen (63%) were evaluated on the same day they commenced treatment, and 11 (37%) were assessed after treatment had begun. Among these 11 participants, four were evaluated one day post-treatment initiation, with the remaining individuals assessed at 3, 4, 6, 12, 15, 19, and 26 days following the start of ADT. For the overall cohort, the median interval between ADT initiation and baseline assessment was 0 days (IQR, 0-1 day; range 0-26 days). Out of the 30 participants enrolled in the study, four dropped out before the 6-month follow-up: two declined to continue follow-up, one moved to a different city, and one discontinued ADT before completing 6 months. Thus, 26 participants completed the clinical follow-up at 6 months. Among these, one participant did not get the final DXA assessment due to a scheduling conflict but completed all clinical and functional assessments (Figure 1).

Demographic and clinical profile

The final cohort consisted of older adults with a predominantly overweight profile and limited ethnic diversity. Cardiometabolic comorbidities were common, particularly arterial hypertension and diabetes mellitus, and several participants presented additional chronic conditions or required concomitant non-oncological medications (Table 1).

Oncological and treatment-related characteristics

Overall, participants predominantly had locally advanced disease, with cT3-cT4 stages being the most common among those with available staging data. Among the 20 participants with available Gleason scores, 10 (50%) had a score of 7, five (25%) a score of 8, and five (25%) a score of 9. ADT was initiated a median of 30.5 months (range 1 – 180) after PCa diagnosis, and the baseline musculoskeletal assessment was performed at or shortly after ADT initiation. Central ADT combined with an ARPI was the predominant treatment regimen (23/30, 76.7%), with apalutamide being the most frequently used ARPI (17/30, 56.7%). No participant received chemotherapy (Table 1).

Body composition and bone mineral density outcomes

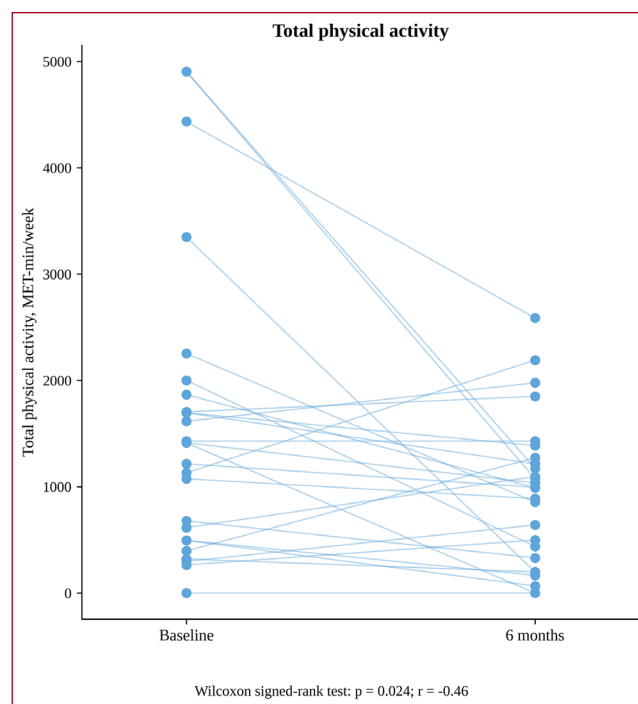
Body mass index remained stable over the 6-month follow-up period ($p = 0.314$), indicating overall weight stability despite significant changes in body composition. A significant unfavorable shift in body composition was observed, characterized by an increase in adiposity and concomitant reduction in lean mass. Specifically, fat mass index, total fat mass, and body fat percentage increased significantly after 6 months of ADT (all $p < 0.001$). Regional analysis demonstrated significant increases in gynoid fat depots ($p < 0.001$), with a concomitant reduction in the android/gynoid fat ratio ($p = 0.003$). In contrast, total lean mass significantly decreased ($p = 0.006$) over time (Table 2).

Regarding skeletal parameters, DXA-based analysis

Table 1. Demographic, clinical, and disease characteristics of the study population (n=30).

Demographic and clinical characteristics	
Age (years), mean $\pm$ SD	70.7 $\pm$ 8.2
Body mass index (kg/m ²), mean $\pm$ SD	26.7 $\pm$ 3.7
Skin color (n, %)	
• White	29 (97%)
• Black	1 (3%)
Comorbidities (n, %)	
• Hypertension	19 (63%)
• Diabetes mellitus	8 (27%)
• Depression/anxiety	3 (10%)
• Cardiac arrhythmia	2 (7%)
• Infectious history (HBV/HIV)	2 (7%)
• Asthma	1 (3%)
Concomitant non-oncologic medications, n (%)	14 (47%)
Prostate cancer characteristics	
Gleason score, n=20 (%)	
• 7	10 (50%)
• 8	5 (25%)
• 9	5 (25%)
Clinical tumor stage, n=24 (%)	
cT3	8 (33%)
cT3a	4 (17%)
cT3b	3 (13%)
cT3/4	1 (4%)
cT4	8 (33%)
Treatment characteristics	
Time from PCa diagnosis to ADT initiation (months), median (range)	30.5 (1-180)
Time from ADT initiation to baseline musculoskeletal assessment (days), median (range)	0 (0-26)
Treatment regimen n (%)	
Central ADT + ARPI	23 (77)
• Apalutamide	17 (57)
• Darolutamide	4 (13)
• Enzalutamide	2 (7)
Central ADT monotherapy	6 (20)
Peripheral antiandrogen monotherapy	1 (3)
Chemotherapy n (%)	0 (0)

Data are presented as n(%) unless otherwise indicated. Denominators other than n=30 are reported for each respective variable. cT3, subtype unspecified' denotes cT3 disease for which the cT3a/cT3b subclassification was unavailable. cT3: extraprostatic extension (T3a) or seminal vesicle invasion (T3b); cT4: tumor fixed or invading adjacent structures beyond the seminal vesicles. PCa, Prostate cancer; ADT, Androgen Deprivation Therapy; ARPI, Androgen Receptor Pathway Inhibitors; HIV, Human Immunodeficiency Virus.

**Figure 2.** Individual changes in total physical activity between baseline and 6 months. Each line represents paired IPAQ measurements from one participant (n=26).

demonstrated significant reductions in bone mineral density at the lumbar spine ($p = 0.002$) and total proximal femur ($p = 0.002$), while no statistically significant change was observed at the femoral neck. Concordantly, T-scores declined significantly at the lumbar spine ($p = 0.003$) and total proximal femur ($p = 0.005$), whereas femoral neck T-score showed no significant change (Table 3).

Muscle mass and strength

At the 6-month assessment, significant declines were observed in both muscle mass and muscle strength. BI/ASMI index decreased significantly ($p = 0.023$), as did handgrip strength ($p < 0.001$) (Table 4).

Physical performance

At the 6-month assessment, functional performance showed no significant changes in TUG ($p = 0.280$) or comfortable ($p = 0.303$) and fast gait speeds ($p = 0.588$) compared with baseline (Table 5).

Postural stability and gait performance

Sway area and RMS acceleration in the anteroposterior (AP) direction increased significantly during quiet standing ($p = 0.004$ and $p = 0.012$, respectively), whereas no

Variable	Baseline	6 months	Paired change (95% CI)	Effect size	p value
BMI (kg/m ²)	26.20 ± 3.57	26.29 ± 3.55	0.0 (0.0 to 0.0)	+0.34	0.314 ¹
Lean mass (kg)	50.79 ± 7.35	49.70 ± 6.75	-1.09 (-1.83 to -0.35)	-0.61	0.006 ²
Fat mass (kg)	25.44 ± 8.50	27.47 ± 8.59	+1.51 (+0.61 to +2.63)	+0.78	<0.001 ¹
FMI (kg/m ²)	8.36 ± 2.58	9.03 ± 2.59	+0.53 (+0.41 to 0.89)	+0.77	<0.001 ¹
Body fat (%)	32.79 ± 6.58	34.99 ± 6.28	+2.20 (+1.25 to +3.15)	+0.95	<0.001 ²
Android fat (%)	38.05 ± 11.30	39.87 ± 10.78	+0.40 (-0.40 to +4.10)	+0.30	0.148 ¹
Gynoid fat (%)	32.69 ± 5.54	36.42 ± 5.16	+3.74 (+2.46 to +5.01)	+1.21	<0.001 ²
Android/gynoid ratio	1.15 ± 0.26	1.08 ± 0.24	-0.08 (-0.12 to -0.05)	-0.58	0.003 ¹

Data are presented as mean ± SD. Paired changes are reported with 95% CIs. Effect sizes are reported as Cohen's *dz* for paired *t*-tests and *r* for Wilcoxon signed-rank tests. Positive and negative values indicate the direction of change. ¹ Wilcoxon signed-rank test; ² paired-samples *t*-test. BMI, body mass index; FMI, fat mass index.

Table 2. Changes in body composition after six months of ADT (n=25).

Variable	Baseline	6 months	Paired change (95% CI)	Effect size	P value
BMD lumbar spine L1-L4 (g/cm ²)	1.207 ± 0.232	1.175 ± 0.227	-0.033 (-0.052 to -0.013)	-0.70	0.002 ²
BMD femoral neck (g/cm ²)	0.915 ± 0.145	0.902 ± 0.151	-0.013 (-0.030 to +0.003)	-0.33	0.111 ²
BMD total proximal femur (g/cm ²)	0.992 ± 0.153	0.969 ± 0.144	-0.020 (-0.030 to -0.010)	-0.65	0.002 ¹
T-score lumbar spine L1-L4	0.376 ± 1.891	0.120 ± 1.829	-0.256 (-0.415 to -0.097)	-0.66	0.003 ²
T-score femoral neck	-0.868 ± 1.055	-0.964 ± 1.099	-0.096 (-0.206 to +0.014)	-0.36	0.083 ²
T-score total proximal femur	-0.120 ± 1.219	-0.216 ± 1.171	-0.100 (-0.200 to -0.100)	-0.62	0.005 ¹

Data are presented as mean ± SD. Paired changes are reported with 95% CIs. Effect sizes are reported as Cohen's *dz* for paired *t*-tests and *r* for Wilcoxon signed-rank tests. Positive and negative values indicate the direction of change. ¹ Wilcoxon signed-rank test; ² paired-samples *t*-test. BMD, Bone Mineral Density.

Table 3. Changes in bone mineral density and T-score after six months of ADT (n=25).

Variable	Baseline	6 months	Paired change (95% CI)	Effect size	n	p value
Handgrip strength (kgf)	38.73 ± 8.56	35.12 ± 8.72	-3.62 (-5.04 to -2.19)	-1.03	26	<0.001
BI/ASMI (kg/m ²)	7.65 ± 1.06	7.44 ± 0.99	-0.20 (-0.38 to -0.03)	-0.49	25	0.023

Data are presented as mean ± SD. BI/ASMI was calculated as appendicular skeletal muscle mass divided by height squared (kg/m²). Paired changes are reported with 95% CIs, and effect sizes are reported as Cohen's *dz* for paired *t*-tests. Positive and negative values indicate the direction of change and *n* represents the number of participants with paired data available for each analysis. BI, Baumgartner Index; ASMI, Appendicular Skeletal Muscle Mass Index.

Table 4. Changes in muscle strength and muscle mass after 6 months of ADT.

Variable	Baseline	6 months	Paired change (95% CI)	Effect size	P value
TUG (s)	12.80 ± 2.80	13.29 ± 2.46	+0.36 (-0.59 to +0.91)	+0.22	0.280 ¹
Comfortable gait speed (m/s)	1.15 ± 0.16	1.13 ± 0.20	-0.030 (-0.137 to +0.036)	-0.21	0.303 ¹
Fast gait speed (m/s)	1.64 ± 0.23	1.61 ± 0.28	-0.024(-0.113 to +0.066)	-0.11	0.588 ²

Data are presented as mean ± SD. Paired changes are reported with 95% CIs. Effect sizes are reported as Cohen's *dz* for paired *t*-tests and *r* for Wilcoxon signed-rank tests. Positive and negative values indicate the direction of change. ¹ Wilcoxon signed-rank test; ² paired-samples *t*-test.

Table 5. Timed Up and Go (TUG) and 10-Meter Walk Test (10MWT) performance at baseline and 6-month follow-up (n = 26).

Task	Variable	Baseline	6 months	Paired change (95% CI)	Effect size	p value
Quiet standing	Area (m ² /s ⁴)	0.049(0.018)	0.060(0.023)	+0.011 (0.004 to 0.018)	+0.62	0.004
	RMS AP (m/s ²)	0.050(0.011)	0.058(0.016)	+0.008 (0.002 to 0.014)	+0.53	0.012
	RMS ML (m/s ²)	0.053(0.011)	0.055(0.012)	+0.002 (-0.001 to 0.005)	+0.30	0.138
	Mean frequency AP (Hz)	0.405(0.115)	0.369(0.131)	-0.036 (-0.088 to 0.016)	-0.28	0.167
	Mean frequency ML (Hz)	0.515(0.116)	0.487(0.114)	-0.028 (-0.079 to 0.023)	-0.22	0.271
Comfortable gait	Cadence (steps/min)	104.138 (8.157)	103.337 (8.816)	-0.801 (-3.304 to 1.702)	-0.13	0.516
	Mean Step Length (m)	0.553 (0.049)	0.541(0.043)	-0.012 (-0.027 to 0.003)	-0.33	0.101
	Mean Step Velocity (m/s)	0.960(0.114)	0.932(0.109)	-0.028 (-0.072 to 0.016)	-0.25	0.206
	Mean Stride Time (s)	1.160(0.102)	1.170(0.112)	+0.010 (-0.019 to 0.039)	+0.14	0.488
Fast gait	Cadence (steps/min)	123.554 (9.863)	122.650(11.719)	-0.904 (-3.836 to 2.028)	-0.12	0.531
	Mean Step Length (m)	0.648(0.058)	0.637(0.064)	-0.011 (-0.032 to 0.010)	-0.21	0.284
	Mean Step Velocity (m/s)	1.336(0.158)	1.306(0.199)	-0.030 (-0.093 to 0.033)	-0.19	0.339
	Mean Stride Time (s)	0.978(0.080)	0.987(0.106)	+0.009 (-0.017 to 0.035)	+0.14	0.482

Data are presented as mean ± SD. Paired changes are reported with 95% CIs, and effect sizes are reported as Cohen's *dz* for paired *t*-tests. Positive and negative values indicate the direction of change. RMS, root mean square.

Table 6. Accelerometer-derived measures of postural control and gait performance at baseline and 6-month follow-up (n = 26).

significant changes were observed in mediolateral (ML) RMS acceleration or mean sway frequency in either direction (all *p* > 0.05). No significant changes were observed in spatiotemporal gait parameters under either comfortable or fast walking conditions (all *p* > 0.05). Overall, accelerometer-based assessment showed changes in selected postural stability parameters, while gait characteristics showed no significant changes at the 6-month assessment (Table 6).

No adverse events occurred during balance, gait, or muscle strength assessments.

Physical activity

A reduction in habitual physical activity was observed over the follow-up period, with IPAQ values decreasing from a median of 1413 MET-min/week (IQR, 525–1825; range, 0 - 4905) to 992 MET-min/week (IQR, 357–1258;

Patient	Age (yrs)	Comfortable gait speed (m/s)		Fast gait speed (m/s)		HGS (kgf)		BI/ASMI (kg/m ²)		TUG (s)		Diagnosis
		Baseline	6 months	Baseline	6 months	Baseline	6 months	Baseline	6 months	Baseline	6 months	
1	82	1.144	0.969	1.423	1.103	30	24	5.84	5.75	17.5	16.1	Sarcopenia
2	74	1.179	1.329	1.964	1.936	29	26	6.04	6.04	10.5	9.6	Sarcopenia

HGS, handgrip strength; BI, Baumgartner Index; ASMI, Appendicular Skeletal Muscle Mass Index; TUG, Timed Up and Go. Sarcopenia was defined according to EWGSOP2¹¹ as the coexistence of low muscle strength (handgrip strength <27kg) and low muscle quantity (BI/ASMI <7.0 kg/m²).

Table 7. Individual muscle and functional parameters at baseline and 6 months (n=2).

Patient	BMD (g/cm ²)				T-score				Final Diagnosis
	Lumbar spine		Femoral neck		Lumbar spine		Femoral neck		
	Baseline	6 months	Baseline	6 months	Baseline	6 months	Baseline	6 months	
1	0.81	0.86	0.60	0.58	-3.1	-2.6	-3.1	-3.3	Osteosarcopenia
2	0.87	0.86	0.71	0.68	-2.6	-2.5	-2.4	-2.6	Osteosarcopenia

Osteoporosis was defined as T-score ≤ -2.5 standard deviations; osteosarcopenia was defined as the coexistence of osteoporosis and sarcopenia^{15,18,28}. BMD, Bone mineral density. Osteosarcopenia incidence: 8.0% (95% CI, 1.0-26.0%).

Table 8. Individual bone parameters at baseline and 6 months and final diagnostic classification (n=2).

range, 0 - 2586). This change reached statistical significance ($p = 0.024$), with a moderate effect size ($r = -0.46$) (Figure 2).

Clinical outcomes

At the 6-month assessment, two participants who did not meet the criteria for sarcopenia at baseline presented both low muscle strength and low appendicular muscle mass, meeting the diagnostic criteria for sarcopenia (Table 7). Both participants had osteoporosis already present at the baseline study DXA and

subsequently developed sarcopenia, thereby meeting the adopted definition of osteosarcopenia at the 6-month assessment (Table 8). Accordingly, incident osteosarcopenia was identified in 2 of 25 participants (8.0%; 95% CI, 1.0% - 26%). No falls or incident fragility fractures were reported during follow-up.

Sensitivity analysis

A sensitivity analysis was performed in the 17 participants who completed the 6-month follow-up and whose baseline assessment occurred on the same day as

ADT initiation. Significant increases in fat mass and body fat percentage and reductions in lean mass, handgrip strength, lumbar spine BMD, and lumbar T-score were maintained. Changes in BI/ASMI and total hip BMD were no longer statistically significant, although their direction was consistent with the primary analysis. TUG and gait speed remained unchanged. Overall, the direction of changes was generally similar to that observed in the primary analysis. Detailed individual results of the sensitivity analysis are provided in Supplementary Tables 1S-3S.

Discussion

In the present prospective observational study, clinically relevant musculoskeletal changes were observed following ADT initiation. At the 6-month assessment, changes were observed across multiple musculoskeletal domains, including increased adiposity, reduced lean mass and muscle strength, bone loss, and increased postural sway. Notably, the changes in body composition occurred despite no significant change in BMI. This apparent dissociation between stable body weight and adverse changes in body composition has also been described in men undergoing ADT, reinforcing that body weight or BMI alone may substantially underestimate the extent of treatment-related musculoskeletal changes²⁹. Although conventional gait parameters showed no significant changes, concurrent changes in muscle and bone parameters were observed at the 6-month assessment, together with changes in selected parameters of postural stability. This pattern is consistent with the contemporary concept of frailty, characterized by reduced physiological reserve, and the coexistence of structural and functional impairments³⁰. These findings were observed in a cohort in which most participants received concomitant ARPI therapy in addition to central ADT and therefore should be interpreted in the context of combined treatment exposure.

One of the most relevant findings of this study was a greater reduction in muscle strength than in muscle mass. While appendicular muscle mass, represented by the BI/ASMI Index, decreased by approximately 3%, handgrip strength declined by more than 9% during the same period. At 6 months, reductions in muscle strength were observed together with changes in muscle quantity. According to the EWGSOP2 framework, muscle strength is the primary determinant of sarcopenia because it more closely reflects functional capacity and predicts adverse clinical outcomes than muscle mass alone. Experimental and clinical evidence has associated androgen deprivation with impaired anabolic signaling, reduced protein synthesis, increased intramuscular fat infiltration (myosteatosis), and neuromuscular dysfunction, all of which may adversely affect muscle quality. Collectively, these alterations may be associated with impaired neuromuscular efficiency and force generation, with reductions in muscle strength reported even in the absence of substantial losses in

muscle mass^{9,12,13}.

Although muscle quality was not directly assessed in the present study, the reduction in handgrip strength despite relatively modest loss of appendicular lean mass is consistent with this biological model and reinforces the importance of evaluating muscle function in addition to muscle quantity during ADT. Muscle quality has emerged as a critical determinant of physical function, integrating structural characteristics, neuromuscular activation, fat infiltration, and contractile efficiency beyond simple muscle quantity. Consequently, preservation of muscle mass does not necessarily imply preservation of muscle function³¹.

The skeletal findings further support the concept that concurrent changes in muscle and bone should not be interpreted as independent processes. Significant reductions in lumbar spine and total hip bone mineral density were observed concurrently with declines in muscle mass and strength, consistent with the concept of an integrated muscle-bone response described during androgen deprivation. Current evidence suggests that osteosarcopenia reflects the convergence of endocrine, inflammatory, metabolic, and mechanical pathways involving both bone and skeletal muscle homeostasis and altered muscle-bone crosstalk¹⁵⁻¹⁷. Rather than representing isolated tissue-specific abnormalities, these alterations appear to reflect a common pattern associated with musculoskeletal vulnerability. This integrated muscle-bone model also reinforces the growing recognition that osteosarcopenia should be interpreted as a systemic syndrome rather than two independent diseases, with shared endocrine, inflammatory, and mechanical mechanisms involving both tissues^{16,17}.

Although only two participants fulfilled formal diagnostic criteria for osteosarcopenia at the 6-month assessment, this finding should be interpreted cautiously. While osteosarcopenia is diagnosed as a categorical clinical entity, its development is likely to reflect a progressive continuum involving both muscle and bone rather than an abrupt event^{15,16}. The relatively low incidence observed in our cohort should be interpreted in the context of the short follow-up duration and small sample size. Indeed, nearly all participants exhibited unfavorable changes in at least one component of the osteosarcopenic spectrum, including muscle strength, lean mass, fat accumulation, bone mineral density, or postural control. Consequently, our findings are better interpreted as suggestive of an osteosarcopenic phenotype.

An additional finding deserving attention was the dissociation between static balance and gait performance. Despite increased postural sway parameters during quiet standing, spatiotemporal gait characteristics remained unchanged under both comfortable and fast walking conditions. This pattern suggests that assessment of static postural control may provide complementary information to conventional gait measures in patients undergoing

ADT. Quiet standing requires continuous sensorimotor integration and fine postural adjustments, whereas habitual gait involves compensatory motor strategies that may contribute to maintaining locomotor performance^{11,12}. Thus, changes in postural stability may be observed in the absence of clinically detectable gait impairment, representing a potentially relevant functional feature of ADT-related musculoskeletal changes.

Conversely, gait speed is influenced by compensatory motor strategies and the relatively low physiological demands of habitual walking³². In the present study, reductions in muscle strength were observed in the absence of significant changes in mean gait performance. These findings are consistent with progressive ADT-related musculoskeletal changes described in recent systematic reviews¹². Walking speed is influenced by multiple physiological systems and may be maintained through compensatory mechanisms despite alterations in other functional domains^{11,32}. The relatively short follow-up period and the overall functional status of our participants may also have limited the detection of clinically detectable changes in gait performance. Reductions in muscle strength and increased postural sway were observed concurrently with no significant changes in mean mobility and gait measures at 6 months.

A significant reduction in habitual physical activity was observed during follow-up. Physical activity may be relevant within the broader context of musculoskeletal status during ADT. Muscle strength and physical activity may be interrelated, with lower activity levels also being associated with muscle atrophy, fat accumulation, bone loss, and functional decline. Although the direction of this relationship cannot be established from the present findings, the observed reduction in physical activity highlights the importance of maintaining regular physical activity throughout treatment³³. Supervised resistance exercise has consistently demonstrated the ability to attenuate reductions in muscle strength and lean mass associated with ADT while improving physical function, supporting its implementation after treatment initiation³⁴.

Rather than representing isolated events, our findings suggest that changes in muscle strength and postural stability, measurable reductions in muscle mass, skeletal changes, and incident osteosarcopenia may represent concurrent components of a broader pattern of musculoskeletal changes. These relationships are biologically plausible and consistent with current evidence describing ADT-related musculoskeletal changes^{12,21}. From a clinical perspective, these findings suggest that musculoskeletal screening should extend beyond measurements of body weight or bone mineral density alone. Assessment of handgrip strength, body composition by DXA, and simple functional tests may contribute to the identification of musculoskeletal changes and support timely preventive interventions. This approach is

consistent with current recommendations emphasizing early recognition of sarcopenia and timely intervention³⁵. Resistance exercise, adequate protein intake, optimization of vitamin D and calcium status, and multidisciplinary management have all shown potential to mitigate ADT-related changes in muscle and bone. Our findings also align with the broader concept of frailty as a reduction in physiological reserve rather than the mere presence of disability. However, in the present study frailty was not assessed using a validated frailty instrument. Therefore, the changes observed in bone, muscle strength, lean mass, and postural stability should not be considered as evidence of a frailty phenotype.

This study has several limitations. Limited statistical power due to the small sample size, the absence of a control group, and single follow-up assessment limit causal inference and generalizability. In some participants, baseline assessment was performed shortly after ADT initiation, and treatment-related changes occurring before baseline measurement therefore cannot be excluded. Given the nature of the study, no single primary outcome was prespecified, and multiple outcomes were examined without adjustment for multiple comparisons; thus, the findings should be interpreted as exploratory. In addition, cancer severity and heterogeneity of ADT regimens may have affected the magnitude of individual responses. Most participants were treated with an ARPI in combination with central ADT. Hence, the observed changes cannot be linked exclusively to ADT, and ARPI exposure should be considered a potential confounding factor. Muscle quality and myosteatosis were not directly assessed, nor were bone turnover biomarkers, advanced measures of bone microarchitecture, or frailty using a validated instrument. The DXA least significant change was not available; therefore, small individual changes in body composition and BMD cannot be distinguished from measurement variability. Falls and physical activity were evaluated using self-report and are therefore susceptible to recall bias. Finally, the small sample recruited within a single healthcare network and the limited ethnic diversity restrict the generalizability of our findings to a broader population. Nevertheless, important strengths of this study include its prospective design and comprehensive, multimodal assessment integrating body composition, bone health, muscle strength, instrumented postural control, gait performance, and physical activity. The simultaneous evaluation of these complementary domains, using objective measures such as DXA, handgrip dynamometry, and triaxial accelerometry, enabled a broad characterization of musculoskeletal and functional changes during ADT, including changes that may not be captured by conventional clinical measures alone.

At 6 months, reductions in muscle strength, muscle mass, and bone parameters and increased postural sway were observed, while gait and mobility measures showed no significant changes. These findings are consistent with

sarcopenic alterations described after initiation of ADT¹² and support the clinical relevance of monitoring musculoskeletal and functional parameters during treatment. Future larger longitudinal studies with longer follow-up and multiple assessment time points, incorporating muscle quality imaging, bone turnover biomarkers, are warranted to further characterize musculoskeletal outcomes during ADT treatment.

Ethics approval

The study protocol was approved by the D'Or Institute for Research and Education (IDOR) Ethics Committee, CAAE: 51989521.5.0000.5249). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all participants before enrollment in the study.

Authors' contributions

R.B. Buksman: Substantial contributions to the conception and design of the study, data acquisition, analysis and interpretation of data; drafting the manuscript; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **V.F. Vianna:** Substantial contributions to the conception and design of the study and interpretation of data; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **E.C. Rodrigues:** Substantial contributions to data acquisition and data analysis; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **T.P. Pinto:** Substantial contributions to data acquisition and interpretation of data; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **F.V. Dos Anjos:** Substantial contributions to data acquisition and interpretation of data; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **A. Couto:** Substantial contributions to data acquisition and data analysis; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **D.R. Filho:** Substantial contributions to data acquisition and interpretation of data; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. **D. Herchenhorn:** Substantial contributions to data interpretation; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to

be accountable for all aspects of the work. M.E.L. Duarte: Substantial contributions to the conception and design of the study, supervision of the research, and interpretation of data; critical revision of the manuscript for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work. All authors reviewed and approved the final text and accept responsibility for the integrity and accuracy of the article's content.

Acknowledgments

The authors used ChatGPT (OpenAI) as a writing assistance tool during the preparation of this manuscript to improve grammar, spelling, readability, overall clarity, to edit successive versions of the text and to assist with the formatting of references. AI was not used to generate, analyze, or interpret data. The suggestions generated by AI were critically reviewed and edited by the authors, who take full responsibility for the accuracy and integrity of the content of the manuscript.

References

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin* 2025;75(1):10-45.
2. Van Blarigan EL, McKinley MA, Washington SL, Cooperberg MR, Kenfield SA, Cheng I, et al. Trends in prostate cancer incidence and mortality rates. *JAMA Netw Open* 2025;8(1):e2456825.
3. Wagle NS, Nogueira L, Devasia TP, Mariotto AB, Yabroff KR, Islami F, et al. Cancer treatment and survivorship statistics, 2025. *CA Cancer J Clin* 2025;75(4):308-40.
4. James ND, Tannock I, N'Dow J, Feng F, Gillessen S, Ali SA, et al. The Lancet commission on prostate cancer: planning for the surge in cases. *Lancet* 2024;403(10437):1683-722.
5. Attard G, Parker C, Eeles RA, Schröder F, Tomlins SA, Tannock I, et al. Prostate cancer. *Lancet* 2016;387(10013):70-82.
6. Litwin MS, Tan HJ. Diagnosis and treatment of prostate cancer. *JAMA* 2017;317(24):2532-42.
7. Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, et al. Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. *N Engl J Med* 2017;377(4):352-60.
8. European Association of Urology. EAU guidelines on prostate cancer 2024. Amhem: EAU Guidelines Office; 2024.
9. Desai K, McManus JM, Sharifi N. Hormonal therapy for prostate cancer. *Endocr Rev* 2021;42(3):354-73.
10. Nguyen PL, Alibhai SM, Basaria S, D'Amico AV, Kantoff PW, Keating NL, et al. Adverse effects of androgen deprivation therapy and strategies to mitigate them. *Eur Urol* 2015;67(5):825-36.
11. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48(1):16-31. Erratum in: *Age Ageing* 2019;48(4):601.
12. Kovač MB, Pavlin T, Čavka L, Ribnikar D, Spazzapan S, Templeton AJ, et al. The trajectory of sarcopenia following diagnosis of prostate cancer: a systematic review and meta-analysis. *J Geriatr Oncol* 2023;14(7):101594.
13. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: systematic review and meta-analysis. *Crit Rev Oncol Hematol* 2020; 145:102839.

14. Compston JE, McClung MR, Leslie WD. Osteoporosis. *Lancet* 2019;393(10169):364-76.
15. Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. *Osteoporos Int* 2017;28(10):2781-90.
16. Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment—facts and numbers. *J Cachexia Sarcopenia Muscle* 2020;11(3):609-18.
17. Yi YT, Zhao HF, Wang WZ, Li X. Osteosarcopenia: epidemiology, molecular mechanisms, and management. *Front Endocrinol (Lausanne)* 2025;16:1577758.
18. Pu Y, Teng Y, Li Y, Zhou Y, Gao M, Yan Z, et al. Osteosarcopenia: key molecular mechanisms and translational perspectives. *Front Physiol* 2026;16:1723522.
19. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* 2005;352(2):154-64.
20. Suarez-Almazor ME, Pundole X, Cabanillas G, Lei X, Zhao H, Elting LS, et al. Association of bone mineral density testing with risk of major osteoporotic fractures among older men receiving androgen deprivation therapy to treat localized or regional prostate cancer. *JAMA Netw Open* 2022;5(4):e225432.
21. Szarzyńska Z, Barczak I, Giermek K, Garczyk A, Mardas M, Stelmach-Mardas M. Influence of androgen deprivation therapy on physical performance and muscle strength in prostate cancer patients: a systematic review. *Rep Pract Oncol Radiother* 2025;30(5):720-31.
22. Mancini M, Salarian A, Carlson-Kuhta P, Zampieri C, King L, Chiari L, et al. ISway: a sensitive, valid and reliable measure of postural control. *J Neuroeng Rehabil* 2012;9:59.
23. Del Din S, Godfrey A, Rochester L. Validation of an accelerometer to quantify a comprehensive battery of gait characteristics in healthy older adults and Parkinson's Disease: toward clinical and at home use. *IEEE J Biomed Health Inform* 2016;20(3):838-47.
24. O'Brien MK, Hidalgo-Araya MD, Mummidisetty CK, Vallery H, Ghaffari R, Rogers JA, et al. Augmenting clinical outcome measures of gait and balance with a single inertial sensor in age-ranged healthy adults. *Sensors (Basel)* 2019;19(20):4537.
25. Moe-Nilssen R. A new method for evaluating motor control in gait under real-life environmental conditions. Part 1: The instrument. *Clin Biomech (Bristol)* 1998;13(4-5):320-7.
26. Oliveira LF, Simpson DM, Nadal J. Calculation of area of stabilometric signals using principal component analysis. *Physiol Meas* 1996;17(4):305-12.
27. Zijlstra W, Hof AL. Assessment of spatio-temporal gait parameters from trunk accelerations during human walking. *Gait Posture* 2003;18(2):1-10.
28. Clynes MA, Gregson CL, Bruyère O, Cooper C, Dennison EM. Osteosarcopenia: where osteoporosis and sarcopenia collide. *Rheumatology (Oxford)* 2021;60(2):529-37.
29. Chiang PK, Tsai WK, Chiu AW, Lin JB, Yang FY, Lee J. Muscle loss during androgen deprivation therapy is associated with higher risk of non-cancer mortality in high-risk prostate cancer. *Front Oncol* 2021;11:722652.
30. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013;381(9868):752-62.
31. Correa-de-Araujo R, Harris-Love MO, Miljkovic I, Fragala MS, Anthony BW, Manini TM. The need for standardized assessment of muscle quality in skeletal muscle function deficit and other aging-related muscle dysfunctions: a symposium report. *Front Physiol* 2017;8:87.
32. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. *JAMA* 2011;305(1):50-8.
33. Galvão DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. *J Clin Oncol* 2010;28(2):340-7.
34. Cormie P, Galvão DA, Spry N, Joseph D, Chee R, Taaffe DR, et al. Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy? A randomised controlled trial. *BJU Int* 2015;115(2):256-66.
35. Bauer J, Morley JE, Schols AMWJ, Ferrucci L, Cruz-Jentoft AJ, Dent E, et al. Sarcopenia: A Time for Action. An SCWD Position Paper. *J Cachexia Sarcopenia Muscle* 2019;10(5):956-61.

Patient ID	BI/ASMI Baseline (kg/m ²)	BI/ASMI 6 months (kg/m ²)	HGS Baseline (kgf)	HGS 6 months (kgf)	Fat mass Baseline (kg)	Fat mass 6 months (kg)	Lean mass Baseline (kg)	Lean mass 6 months (kg)	Total fat Baseline (%)	Total fat 6 months (%)
5	6.87	7.24	40	33	25.94	27.31	47.79	49	35.2	35.8
7	6.29	7.03	33	28	27.13	27.74	45.95	46.2	37.1	37.5
8	7.91	7.5	40	37	51.04	50.75	57.15	54.49	47.2	48.2
9	7.21	6.78	33	31	26.48	26.7	48.49	47.72	35.3	35.9
10	8.32	8.17	40	37	16.09	17.6	49.55	48.35	24.5	26.7
11	8.5	8.74	38	42	28.35	35.32	57.85	54.98	32.9	39.1
13	7.72	7.62	29	28	23.62	26.77	50.91	51.52	31.7	34
15	5.84	5.75	30	24	11.66	13.21	40.89	41.28	22.2	24.3
16	8.48	7.82	38	34	32.69	35.19	62.88	59.96	34.2	37
17	7.35	7.45	35	35	20.91	20.99	44.52	43.2	32	32.7
19	8.73	8.31	34	32	29.1	38.03	59.67	58.04	32.8	39.6
22	7.45	7.76	34	34	16.71	15.62	46.34	48.63	26.5	24.3
24	7.84	6.98	34	31	25.76	30.16	46.94	42.26	35.4	41.7
25	7.07	6.95	32	32	27.6	28.96	48.38	47.53	36.3	37.9
26	9.4	9.1	46	36	36.88	38.14	61.22	59.35	37.6	39.1
27	7.78	7.77	37	31	31.61	31.76	51.46	51.46	38.1	38.2
29	10.33	9.4	71	69	11.45	15.88	67.84	66.25	14.4	19.3

The sensitivity analysis included participants who completed the 6-month follow-up and whose baseline assessment was performed on the same day as ADT initiation. BI, Baumgartner Index; ASMI, appendicular skeletal muscle mass index; HGS, handgrip strength.

Supplementary Table 1. Individual baseline and 6-month follow-up muscle and body composition parameters in participants included in the sensitivity analysis (n=17).

Patient ID	BMD Lumbar Baseline (g/cm ²)	BMD Lumbar 6 months (g/cm ²)	BMD Neck Baseline (g/cm ²)	BMD Neck 6 months (g/cm ²)	BMD proximal femur Baseline (g/cm ²)	BMD proximal femur 6 months (g/cm ²)	T-score lumbar Baseline (SD)	T-score lumbar 6 months (SD)	T-score neck Baseline (SD)	T-score neck 6 months (SD)	T-score proximal femur Baseline (SD)	T-score proximal femur 6 months (SD)
5	1.54	1.4	0.86	0.89	1.07	1.08	3.1	2	-1.2	-1.1	0.5	0.6
7	1.3	1.31	0.73	0.77	0.78	0.79	1.1	1.2	-2.2	-1.9	-1.8	-1.7
8	1.45	1.47	1.29	1.38	1.31	1.31	2.3	2.5	1.9	2.5	2.4	2.4
9	1	0.97	0.97	0.88	1.02	0.99	-1.4	-1.6	-0.5	-1.1	0.1	-0.1
10	1.15	1.14	0.87	0.84	0.94	0.92	-0.2	-0.3	-1.2	-1.4	-0.5	-0.6
11	1.47	1.42	1.07	1.03	1.16	1.13	2.6	2.1	0.3	0	1.3	1
13	1.1	1.04	0.85	0.84	0.95	0.95	-0.6	-1.2	-1.3	-1.4	-0.4	-0.4
15	0.81	0.86	0.6	0.58	0.7	0.7	-3.1	-2.6	-3.1	-3.3	-2.4	-2.5
16	1.09	1.08	0.89	0.87	0.89	0.9	-0.7	-0.8	-1.1	-1.2	-0.9	-0.9
17	1.22	1.2	1.17	1.17	1.18	1.16	0.5	0.3	1	1	1.4	1.2
19	1.24	1.16	1.03	0.93	1.07	1.04	0.5	-0.2	-0.1	-0.7	0.5	0.3
22	0.9	0.85	0.85	0.86	0.78	0.85	-2.4	-2.8	-1.3	-1.3	-1.8	-1.3
24	1.358	1.29	0.95	0.96	1.04	1.01	1.5	0.9	-0.6	-0.6	0.2	0
25	1.62	1.6	1.02	1.02	1.21	1.2	3.6	3.4	-0.1	-0.1	1.6	1.5
26	1.4	1.3	0.89	0.88	1.02	1	1.9	1.5	-1.1	-1.1	0.1	0
27	0.91	0.9	0.76	0.77	0.81	0.8	-2.3	-2.3	-2	-1.9	-1.6	-1.6
29	1.12	1.07	0.98	0.93	1.16	1.13	-0.5	-0.9	-0.4	-0.8	1.2	1

The sensitivity analysis included participants who completed the 6-month follow-up and whose baseline assessment was performed on the same day as ADT initiation. BMD, bone mineral density.

Supplementary Table 2. Individual baseline and 6-month follow-up DXA-derived bone parameters in participants included in the sensitivity analysis (n=17).

Patient ID	TUG Baseline (s)	TUG 6 months (s)	Gait speed (comfortable) Baseline (m/s)	Gait speed (comfortable) 6 months (m/s)	Gait speed (fast) Baseline (m/s)	Gait speed (fast) 6 months (m/s)
5	12.52	10.76	1.227	1.057	1.7	1.703
7	15.53	17.78	0.999	1.074	1.394	1.323
8	11.98	11.29	1.257	1.111	1.713	1.612
9	6.43	13.53	1.321	1.046	2.195	2.111
10	9.65	12.51	1.214	1.078	1.702	1.646
11	13.98	15.02	1.195	1.257	1.734	1.806
13	14.89	14.76	1.221	0.964	1.526	1.246
15	17.54	16.13	1.144	0.968	1.423	1.103
16	17.48	17.73	0.872	0.919	1.561	1.154
17	16.5	18.31	1.086	0.958	1.615	1.339
19	10.95	12.69	1.254	1.904	1.289	1.745
22	12.17	12.18	0.811	1.168	1.876	1.955
24	13.6	12.18	1.01	1.116	1.558	1.676
25	10.78	13.25	1.194	1.166	1.47	1.488
26	9.95	11.68	1.257	1.225	1.777	1.865
27	17.21	13.44	1.072	1.078	1.601	1.318
29	10.29	11.2	1.367	1.403	1.769	1.888

The sensitivity analysis included participants who completed the 6-month follow-up and whose baseline assessment was performed on the same day as ADT initiation. TUG, Timed Up and Go.

Supplementary Table 3. Individual baseline and 6-month follow-up functional parameters in participants included in the sensitivity analysis (n=17).