

# Resistance Training and Reduction of Treatment Side Effects in Prostate Cancer Patients

DANIEL A. GALVÃO<sup>1</sup>, KAZUNORI NOSAKA<sup>1</sup>, DENNIS R. TAAFFE<sup>2</sup>, NIGEL SPRY<sup>3,4</sup>, LINDA J. KRISTJANSON<sup>5</sup>, MICHAEL R. MCGUIGAN<sup>1</sup>, KATSUHIKO SUZUKI<sup>6</sup>, KANEMITSU YAMAYA<sup>7</sup>, and ROBERT U. NEWTON<sup>1</sup>

<sup>1</sup>*School of Exercise, Biomedical and Health Sciences, Edith Cowan University, Joondalup, AUSTRALIA;* <sup>2</sup>*School of Human Movement Studies, The University of Queensland, Brisbane, AUSTRALIA;* <sup>3</sup>*Department of Radiation Oncology, Sir Charles Gairdner Hospital, Nedlands, AUSTRALIA;* <sup>4</sup>*Faculty of Medicine, University of Western Australia, Nedlands, AUSTRALIA;* <sup>5</sup>*WA Centre for Cancer and Palliative Care, Edith Cowan University, Churchlands, AUSTRALIA;* <sup>6</sup>*Consolidated Research Institute for Advanced Science and Medical Care, Waseda University, JAPAN;* and <sup>7</sup>*Oyokyo Kidney Research Institute, JAPAN*

## ABSTRACT

GALVÃO, D. A., K. NOSAKA, D. R. TAAFFE, N. SPRY, L. J. KRISTJANSON, M. R. MCGUIGAN, K. SUZUKI, K. YAMAYA, and R. U. NEWTON. Resistance Training and Reduction of Treatment Side Effects in Prostate Cancer Patients. *Med. Sci. Sports Exerc.*, Vol. 38, No. 12, pp. 2045–2052, 2006. **Purpose:** To examine the effect of progressive resistance training on muscle function, functional performance, balance, body composition, and muscle thickness in men receiving androgen deprivation for prostate cancer. **Methods:** Ten men aged 59–82 yr on androgen deprivation for localized prostate cancer undertook progressive resistance training for 20 wk at 6- to 12-repetition maximum (RM) for 12 upper- and lower-body exercises in a university exercise rehabilitation clinic. Outcome measures included muscle strength and muscle endurance for the upper and lower body, functional performance (repeated chair rise, usual and fast 6-m walk, 6-m backwards walk, stair climb, and 400-m walk time), and balance by sensory organization test. Body composition was measured by dual-energy x-ray absorptiometry and muscle thickness at four anatomical sites by B-mode ultrasound. Blood samples were assessed for prostate specific antigen (PSA), testosterone, growth hormone (GH), cortisol, and hemoglobin. **Results:** Muscle strength (chest press, 40.5%; seated row, 41.9%; leg press, 96.3%;  $P < 0.001$ ) and muscle endurance (chest press, 114.9%; leg press, 167.1%;  $P < 0.001$ ) increased significantly after training. Significant improvement ( $P < 0.05$ ) occurred in the 6-m usual walk (14.1%), 6-m backwards walk (22.3%), chair rise (26.8%), stair climbing (10.4%), 400-m walk (7.4%), and balance (7.8%). Muscle thickness increased ( $P < 0.05$ ) by 15.7% at the quadriceps site. Whole-body lean mass was preserved with no change in fat mass. There were no significant changes in PSA, testosterone, GH, cortisol, or hemoglobin. **Conclusions:** Progressive resistance exercise has beneficial effects on muscle strength, functional performance and balance in older men receiving androgen deprivation for prostate cancer and should be considered to preserve body composition and reduce treatment side effects. **Key Words:** MUSCLE STRENGTH, SARCOPENIA, ANDROGEN DEPRIVATION, ELDERLY MEN

The use of androgen-deprivation therapy (ADT) in the form of gonadotropin-releasing hormone (GnRH) agonists for prostate carcinoma has increased extensively across all stages and histologic grades of prostate cancer in the past decade (4,18). However, the reduction in testosterone levels by ADT is accompanied by a number of adverse side effects (2,3,6,17,19,23). Some of these side effects include reduced muscle strength, reduced lean and bone mass,

increased fat mass (FM), increased risk of fracture, unfavorable lipid profile, and depression compromising physical and physiological function (12,17,19,20,24). Importantly, these side effects are closely related to an increased risk of developing other chronic conditions (3,17,19). Increases of approximately 7–10% in FM and decreases of approximately 2–4% in lean mass (LM) after 1 yr of ADT have been reported in recent studies (12,14,20,21), as well as reduced muscle strength (2). Additionally, substantial decreases in trabecular and cortical bone mass have been found after administration of ADT, with a concomitant increased risk for fracture at multiple skeletal sites (17,22). As a result, strategies to preserve body composition and improve physical function may reduce the risks of falls, fracture, and subsequent complications.

Existing treatments to alleviate these side effects have been predominantly pharmaceutical; however, these treatments are expensive, and their effects do not translate into improved physical and functional capacity. To date, most of the experimental studies examining the role of exercise

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Address for correspondence: Daniel A. Galvão, Ph.D., School of Exercise, Biomedical and Health Sciences, Edith Cowan University, 100 Joondalup Drive, Joondalup, Western Australia 6027, AUSTRALIA; E-mail: d.galvao@ecu.edu.au.

Submitted for publication March 2006.

Accepted for publication May 2006.

0195-9131/06/3812-2045/0

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DOI: 10.1249/01.mss.0000233803.48691.8b

during cancer treatments have included breast cancer patients and aerobic exercise rather than resistance exercise (5,9). In view of the extensive scientific literature supporting resistance training as the most effective exercise mode for improving muscle strength and physical function and counteracting sarcopenia in older adults (7,8,26), resistance exercise may have a significant role in preventing the catabolic effects of ADT by promoting a sufficient anabolic environment, which can lead to positive musculoskeletal benefits and enhanced physical function.

Segal and associates (16) recently reported positive changes in quality of life and fatigue outcomes subsequent to a short-term resistance training program in prostate cancer patients undertaking testosterone suppression. However, questions remain regarding the adaptive response of specific physiological and physical parameters, such as body composition, muscle hypertrophy, bone mineral density (BMD), functional performance, and balance in a longer-term trial in this population. We therefore designed a nonrandomized clinical trial to examine the possible effects of a 20-wk high-intensity progressive resistance training program on muscle function, functional performance, balance, body composition, and muscle thickness in older men receiving ADT for prostate cancer.

## METHODS

Ninety-one prostate cancer patients who were referred by oncologists and urologists or who responded to advertisements via local newspaper and radio in the city of Perth, Western Australia from February through July 2005, were initially screened for participation in the study (Fig. 1). Exclusion criteria included no histologically documented prostate cancer; not receiving ADT in the previous 2 months; not scheduled to receive ADT for the subsequent 5 months; metastatic disease; any musculoskeletal, cardiovascular, or neurological disorder that could inhibit them from exercising; inability to walk 400 m or undertake upper- and/or lower-limb exercise; resistance training in the previous 12 months; and unwillingness to undertake 20 wk of resistance training. Eleven men were eligible and were invited for familiarization sessions. One subject withdrew from the study at week 7 because of an acute respiratory infection that resulted in several weeks of hospitalization (Fig. 1). Before participation, all subjects obtained medical clearance from their physicians and completed a health history questionnaire. Regarding the activity levels of the subjects before entering the intervention, seven men were not undertaking any form of structured exercise, one was a regular walker, one a regular

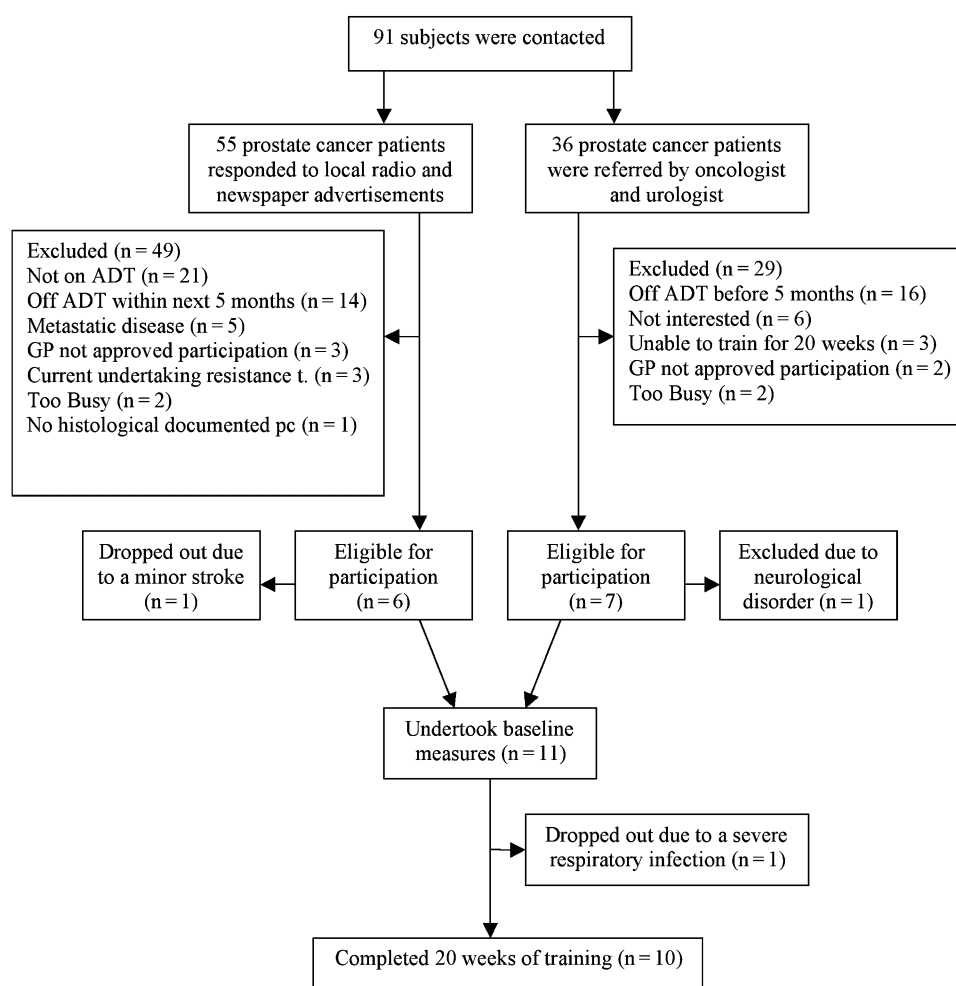


FIGURE 1—Recruitment and flow of participants through the exercise study.

walker and jogger, and one was a recreational bowler. The study was approved by the university human research ethics committee, and all subjects provided written informed consent.

## Training Program

Ten subjects undertook 20 wk of high-intensity progressive resistance training twice a week for 20 wk. The initial 10 wk provided an introductory resistance exercise phase consisting of hydraulic resistance training machines (Isotonic, Fitness Technology, Australia) that are simple and time efficient to use and that provide exclusively concentric muscle contractions, which are likely to facilitate training initiation in this clinical group of men. The exercises included the chest press, seated row, shoulder press, lat pull-down, triceps extension, biceps curl, leg press, squat, leg extension, leg curl, abdominal crunch, and back-extension exercises. In the following 10 wk, the training program was altered to isotonic resistance, which provides concentric and eccentric muscle contractions using similar exercises on different apparatus (Cybex, Strength Equipment). During this period, the lat pull-down and shoulder-press exercises were alternated with the biceps curl and triceps-extension exercises every other session to maintain an exercise session length of 1 h. In every session, general flexibility exercises as well as one set for the first upper- and lower-body exercise at a lower training intensity were undertaken to ensure adequate warm-up before the training program. Both training phases were designed to progress from 12- to 6RM for two to four sets per exercise. Briefly, both training phases were designed as weeks 1–2 (two sets of 12RM), weeks 3–4 (three sets of 10RM), weeks 5–7 (three sets of 8RM), and weeks 8–10 (four sets of 6RM) and were based on the American College of Sports Medicine position stand on progression models in resistance training for healthy adults (13). All sessions were conducted in small groups of one to four participants under direct supervision to ensure safety, proper intensity, and appropriate exercise technique. Additionally, all participants recorded their training weights, number of repetitions, and sets performed in an individual exercise log to ensure adequate progression.

## Muscle Function

Measures of muscle function included dynamic isotonic muscle strength, and endurance was assessed at baseline, week 10, and week 20.

**Dynamic isotonic muscle strength.** Participants underwent two familiarization sessions that included instruction regarding correct exercise technique and practice performing two sets of 12 repetitions on all hydraulic resistance machines in addition to the chest-press, seated row, and leg-press isotonic resistance machines before muscle strength was determined. Dynamic isotonic muscle strength for the chest press, seated row, and leg press were measured using 1RM, as described

previously (27). The 1RM is the maximal weight an individual can move through a full range of motion by maintaining proper exercise technique and not changing body position other than for the specific exercise motion.

The coefficient of variation in our laboratory for repeated 1RM measures performed approximately 1 wk apart was 2.2–7.5%.

**Dynamic isotonic muscle endurance.** Muscle endurance was measured using the maximal number of repetitions performed at 70% of 1RM for the chest-press and leg-press exercises (11). For week 10 and week 20 assessments, the baseline and either the week 10 or final 1RM value, respectively, were used to determine the resistance. The coefficients of variation performed approximately 1 wk apart for the chest-press and leg-press muscle endurance tests were 6.3 and 6.8%, respectively.

## Physical Performance

A battery of tests was used to assess functional performance at baseline, week 10, and week 20. Tests were performed in triplicate (except for the 400-m walk), with sufficient recovery time between trials (11). The fastest time recorded was used in the analyses.

**Chair rise to standing.** Subjects were seated in a hard-backed chair, with a seat height of 43 cm from the floor, with their arms folded across their chest. They were instructed to rise as fast as possible to a full standing position and then return to a full sitting position five times (11,27). The coefficient of variation in our laboratory for the repeated chair rise was 5.6%.

**6-m walk.** Two measures of gait speed were undertaken: usual pace, in which subjects were instructed to walk at a pace similar to what they would use during common daily events; and a fast pace (7). Time taken was determined using two timing gates (Swift Performance Equipment, NSW, Australia). The coefficients of variation in our laboratory for usual and fast walk were 5.6 and 6.7%, respectively.

**6-m backwards walk.** As a measure of dynamic balance, subjects walked backwards for 6 m, placing one foot directly behind the heel of the other with the shoes touching (7,27). Time taken was assessed using timing gates. Subjects were spotted by an investigator, and if they deviated from the line (lost their balance), they were instructed to move back to the line and continue the test, increasing the time required. The coefficient of variation in our laboratory for the backward walk was 9.4%.

**Stair climb.** Subjects were instructed to climb a flight of stairs (13 stairs per flight, 17-cm rise per stair) as rapidly as they could safely manage without use of the handrails (11). Two subjects required the use of the handrails to perform this test. The coefficient of variation in our laboratory for the stair climbing was 4.8%.

**400-m walk.** For the test of walking endurance, participants were required to walk 400 m, which consisted of 10 laps out and back on a 20-m course, as fast as they could at a pace they could maintain for the distance

(11,28). The coefficient of variation in our laboratory for the 400-m walk was 2.5%.

## Sensory Organization Test

The sensory organization test (SOT) was measured using the Neurocom Smart Balance Master (Neurocom International, Inc.). SOT consists of averaging three equilibrium scores for six trial conditions. Subjects stood on the Neurocom force plate without socks or any footwear and with a security belt attached (in case of a fall). According to the manufacturer's protocol and previous studies (29), subjects undertook three 20-s trials for each of the following conditions: 1) eyes open, fixed support surface and surround (visual, vestibular, and somatosensory input); 2) eyes closed, fixed support surface and surround (absent of visual input); 3) eyes open, fixed support surface, and sway-referenced surround (visual input imprecise); 4) eyes open, fixed surround, and sway-referenced support surface (somatosensory inputs imprecise); 5) eyes closed, fixed surround, and sway-referenced support surface (somatosensory inputs imprecise and absent of visual input); and 6) eyes open, sway-referenced support surface and surround (imprecise somatosensory and visual inputs). The equilibrium score was reported as a value between 0 and 100, with 0 indicating a large sway and loss of balance and 100 indicating perfect stability. The coefficient of variation for the SOT was 1.5%.

## Body Composition, BMC, and BMD

BMD ( $\text{g}\cdot\text{cm}^{-2}$ ) of the hip (femoral neck, trochanter, and Ward's triangle) and total-body bone mineral content (BMC, g) were assessed by dual-energy x-ray absorptiometry (DXA; Norland XR-36). In addition, bone mineral-free LM, FM, and percent fat were derived from the whole-body scan. The whole-body scan was performed at baseline, week 10, and week 20, and the hip scan was performed at baseline and week 20. Coefficients of variation in our laboratory (duplicate scans with repositioning) for body composition components were less than 1.0%.

## Muscle Thickness

Muscle thickness was assessed using B-mode ultrasound (Aloka, SSD-500, Tokyo, Japan) at four anatomic sites (anterior (biceps brachii) and posterior (triceps brachii) upper arm at 60% distal between the lateral epicondyle of the humerus and the acromial process of the scapula; anterior (vastus lateralis and rectus femoris) and posterior (biceps femoris) thigh at 70% thigh length between the greater trochanter and lateral condyle of the femur), using methods similar to those described previously by Abe et al. (1). A 5-MHz scanning probe coated with water-soluble gel was placed on the skin, perpendicular to the tissue interface. The subject was seated during the upper-limb measurement, with the elbow extended and relaxed; and in a standing position during the lower-limb measurement, with the knee extended and relaxed. The muscle thickness measurement was extracted from the ultrasonic image, with the distance between the subcutaneous adipose tissue–muscle interface to the muscle–bone interface taken as muscle thickness (1). Two muscle thickness measurements were obtained at each of the four sites and averaged to attain the final value. Great care was taken in marking the skin via anthropometric techniques, and printed images of baseline measures were available during the week 10 and week 20 repeated measurements to ensure that identical sites were assessed.

The coefficient of variation for muscle thickness using repeated ultrasound images in our laboratory was less than 3.5%.

## Blood Sampling

Venous blood samples were drawn from a forearm vein at a fixed time (8:30 a.m. to 10:00 a.m.) at baseline, week 10, and week 20 into sterile vacutainers containing  $\text{K}_2$ -EDTA and serum-separation tubes (Becton Dickinson, Franklin Lakes, NJ). The blood corrected by  $\text{K}_2$ -EDTA tube was used for the measurement of hemoglobin concentration by an automatic full-blood count analyzer (Sysmex XE-AlphaN, Sysmex Corporation, Kobe, Japan). The serum-separation tubes were left at room

TABLE 1. Subjects' baseline characteristics.

Subject	Age (yr)	Diagnosis (d)	ADT (d)	Free Testosterone ( $\text{pg}\cdot\text{mL}^{-1}$ )	PSA ( $\text{ng}\cdot\text{mL}^{-1}$ )	Weight (kg)	BMI ( $\text{kg}\cdot\text{m}^{-2}$ )	Type of ADT
1	79	336	65*	0.79	20.30	66.9	24.3	LHRHa+A
2	65	92	88*	0.26	0.83	73.0	26.8	LHRHa
3	72	184	120*	7.99	1.20	96.7	31.9	LHRHa
4	66	363	210*	0.35	0.04	97.3	32.1	LHRHa
5	59	365	300*	0.15	0.03	68.1	21.2	LHRHa+A
6	72	732	420†	0.87	0.05	75.8	26.2	LHRHa
7	62	2520	720†	9.96	0.04	88.6	29.9	A
8	82	1821	1622†	0.65	2.70	69.9	24.2	LHRHa
9	63	3605	3240†	0.37	3.60	85.6	28.5	LHRHa+A
10	73	3960	3955†	0.35	11.80	76.8	28.0	LHRHa+A
Min	59	92	65	0.15	0.04	66.9	21.2	—
Max	82	3960	3955	9.96	20.30	97.3	32.1	—
Mean	70.3	1397.8	1135.6	2.13	3.09	80.2	27.4	—
SD	8.3	1481.8	1360.4	3.64	6.58	10.9	3.3	—

BMI, body mass index; LHRHa, luteinizing hormone-releasing hormone agonist; A, antiandrogen.

\* Acute ADT; † chronic ADT.



TABLE 2. Muscle strength and endurance at baseline and after 10 and 20 wk of resistance training (mean  $\pm$  SD).

Variable	Baseline	Week 10	Week 20	Percentage Change	P value
Chest press 1RM (kg)	30.9 $\pm$ 13.2	39.5 $\pm$ 15.4 <sup>a</sup>	43.0 $\pm$ 16.4 <sup>b,c</sup>	40.5 $\pm$ 18.5	<0.001
Seated row 1RM (kg)	36.4 $\pm$ 7.3	44.6 $\pm$ 7.3 <sup>a</sup>	50.7 $\pm$ 7.6 <sup>b,c</sup>	41.9 $\pm$ 21.4	<0.001
Leg press 1RM (kg)	81.3 $\pm$ 34.2	109.0 $\pm$ 37.0 <sup>a</sup>	158.0 $\pm$ 63.1 <sup>b,c</sup>	96.3 $\pm$ 25.7	<0.001
Chest press end (rep)	9.0 $\pm$ 2.5	13.8 $\pm$ 2.2 <sup>a</sup>	20.2 $\pm$ 5.5 <sup>b,c</sup>	114.9 $\pm$ 42.6	<0.001
Chest press end†(rep)	9.0 $\pm$ 2.5	7.3 $\pm$ 2.2	9.4 $\pm$ 2.0	3.2 $\pm$ 31.7	0.085
Leg press end (rep)	20.3 $\pm$ 7.9	35.8 $\pm$ 10.8 <sup>a</sup>	47.2 $\pm$ 10.5 <sup>b</sup>	167.1 $\pm$ 143.6	<0.001
Leg press end†(rep)	20.3 $\pm$ 7.9	25.0 $\pm$ 8.4	27.2 $\pm$ 8.6 <sup>b</sup>	56.3 $\pm$ 94.5	0.024

Significant difference,  $P < 0.05$ ; <sup>a</sup> baseline to week 10; <sup>b</sup> baseline to week 20; <sup>c</sup> week 10 to week 20.

1RM, one-repetition maximum; end, muscle endurance at baseline test 70% 1RM; rep, number of repetitions performed.

† Muscle endurance at posttest 70% 1RM.

temperature for the blood to clot and were centrifuged for 10 min at 3000 rpm at 4°C. The serum samples were stored in 0.7-mL aliquots at  $-80^{\circ}\text{C}$  until the day of analysis for prostate specific antigen (PSA), free testosterone, growth hormone (GH), and cortisol concentrations.

### Analysis of PSA, Serum Hormones, and Hemoglobin

PSA was measured by an Immurise analyzer (Beckman Coulter Inc., Fullerton, CA) using a test kit (Diagnostic Products Corporation, Los Angeles, CA). Serum concentrations of the hormones were determined by RIA using a test kit (free testosterone: DPC free testosterone kit, Diagnostic Products Corporation, Los Angeles, CA; GH: GH Kit, SRL Co., Tokyo, Japan; cortisol: Cortisol Kit, Immunotech, Beckman Coulter Inc., Prague, Czech Republic).

### Statistical Analyses

Data were analyzed using SPSS (version 11.0, SPSS Inc, Chicago, IL) statistical software package and included standard descriptive statistics and analyses of variance (ANOVA) and covariance (ANCOVA). Repeated-measures ANOVA was used to compare subjects for the three time points, and ANCOVA was used to compare responses at week 20, adjusted for the baseline value, between acute ( $< 12$  months) and chronic ( $> 12$  months) users of ADT. Where appropriate, the Fisher Protected LSD test was employed to locate the source of significant differences. An alpha level of 0.05 was required for significance, and results are given as means  $\pm$  SD. The statistical power to detect change in the primary study outcomes (physical and functional performance) during the 20-wk intervention ranged from 0.75 to 1.0.

## RESULTS

Subject characteristics are shown in Table 1. All men were receiving ADT before entry to the study for a mean duration of  $1135 \pm 1360$  days. Six men were on GnRH agonists, four men were on maximal blockage therapy (GnRH agonists + antiandrogens), and one was on antiandrogens. Five men were on acute ADT (initiating ADT within the last 12 months, mean  $156 \pm 97$  d), and the remaining six were on chronic ADT (receiving ADT for 12 months or longer, mean  $1951 \pm 1391$  d). All subjects were treated with ADT during the entire course of the study (including pre-, mid-, and posttest measures and for all 40 training sessions) for a 6-month period.

### Dynamic Muscle Strength and Muscle Endurance

Baseline, week 10, week 20 and percentage change in muscle strength and endurance values are reported in Table 2. There was a significant increase in strength for all three exercises, with a continuous improvement for both upper- and lower-body strength from baseline to weeks 10 and 20 ( $P < 0.001$ ). Similarly, upper- and lower-body muscle endurance (number of repetitions performed) increased ( $P < 0.001$ ) when 70% of the 1RM baseline load was used during retesting. Muscle endurance assessed using 70% of the 1RM posttest load also increased ( $P = 0.024$ ) for the leg-press exercise and approached significance ( $P = 0.085$ ) for the chest press.

### Physical Performance and SOT

After the 20-wk training period, there was a significant improvement ( $P < 0.05$ ) in the chair rise, 6-m usual walk speed, backward walk speed, 400-m corridor walk, and stair climbing test (Table 3). Additionally, the changes in

TABLE 3. Functional performance measures and sensory organization test (SOT) at baseline and after 10 and 20 wk of resistance training (mean  $\pm$  SD).

Variable	Baseline	Week 10	Week 20	Percentage Change	P Value
Chair rise (s)	15.4 $\pm$ 4.9	11.3 $\pm$ 3.5 <sup>a</sup>	10.5 $\pm$ 2.7 <sup>b</sup>	-26.8 $\pm$ 7.1	<0.001
6-m backwards walk (s)	23.5 $\pm$ 9.3	18.7 $\pm$ 10.1	17.7 $\pm$ 10.1 <sup>b</sup>	-22.3 $\pm$ 21.9	0.017
6-m usual walk (s)	5.0 $\pm$ 1.0	4.5 $\pm$ 0.8 <sup>a</sup>	4.3 $\pm$ 0.7 <sup>b</sup>	-14.1 $\pm$ 10.2	0.002
6-m fast walk (s)	3.7 $\pm$ 0.7	3.5 $\pm$ 0.7	3.5 $\pm$ 0.7	-5.5 $\pm$ 10.4	0.227
400-m walk (s)	283.1 $\pm$ 60.0	255.6 $\pm$ 40.8 <sup>a</sup>	252.1 $\pm$ 46.5 <sup>b,c</sup>	-7.4 $\pm$ 5.9	0.003
Stair climb (s)	7.0 $\pm$ 3.6	6.5 $\pm$ 3.9 <sup>a</sup>	6.3 $\pm$ 2.9 <sup>b</sup>	-10.4 $\pm$ 9.8	0.014
SOT (0-100)	68.7 $\pm$ 8.3	72.7 $\pm$ 6.1	75.7 $\pm$ 6.9 <sup>b</sup>	7.8 $\pm$ 6.9	0.042

Significant difference,  $P < 0.05$ ; <sup>a</sup> baseline to week 10; <sup>b</sup> baseline to week 20; <sup>c</sup> week 10 to week 20.

TABLE 4. Body composition, whole-body bone mass, hip BMD, and muscle thickness at baseline and after 10 and 20 wk of resistance training (mean  $\pm$  SD).

Variable	Baseline	Week 10	Week 20	Percentage Change	P Value
Bone mineral-free lean mass (kg)	52.2 $\pm$ 5.6	52.2 $\pm$ 5.8	52.0 $\pm$ 5.7	-0.4 $\pm$ 2.2	0.844
Fat mass (kg)	25.7 $\pm$ 8.5	25.0 $\pm$ 8.5	24.9 $\pm$ 8.4	-0.0 $\pm$ 6.1	0.823
Percent body fat	30.7 $\pm$ 7.2	30.5 $\pm$ 6.7	30.6 $\pm$ 6.7	0.3 $\pm$ 5.3	0.852
Total BMC (g)	3055.5 $\pm$ 396.4	3073.1 $\pm$ 430.7	3063.2 $\pm$ 410.2	0.2 $\pm$ 2.5	0.763
Fem neck BMD (g·cm <sup>-2</sup> )	0.868 $\pm$ 0.123	—	0.880 $\pm$ 0.115	1.6 $\pm$ 5.3	0.422
Trochanter BMD (g·cm <sup>-2</sup> )	0.817 $\pm$ 0.110	—	0.820 $\pm$ 0.124	0.3 $\pm$ 4.7	0.806
Wards triangle BMD (g·cm <sup>-2</sup> )	0.590 $\pm$ 0.124	—	0.596 $\pm$ 0.145	0.8 $\pm$ 7.0	0.751
Biceps thickness (cm)	2.69 $\pm$ 0.54	2.83 $\pm$ 0.43	2.91 $\pm$ 0.57	3.5 $\pm$ 6.9	0.621
Triceps thickness (cm)	1.94 $\pm$ 0.26	2.22 $\pm$ 0.51	2.33 $\pm$ 0.49	5.5 $\pm$ 17.0	0.875
Quadriceps thickness (cm)	2.15 $\pm$ 0.30	2.24 $\pm$ 0.42	2.46 $\pm$ 0.41 <sup>a</sup>	15.7 $\pm$ 12.1	0.050
Hamstrings thickness (cm)	4.52 $\pm$ 0.74	4.31 $\pm$ 0.99	4.53 $\pm$ 0.89	0.2 $\pm$ 10.0	0.483

<sup>a</sup> Baseline to week 20,  $P < 0.05$ .

the chair rise, stair climbing, 6-m usual walk, and 400-m walk time were significantly different between baseline and week 10. There was also a significant increase in the SOT equilibrium score ( $P = 0.042$ ).

### Body Composition, BMC, BMD and Muscle Thickness

There was no change for LM, FM, percent body fat, whole-body BMC, or hip BMD (Table 4); however, quadriceps muscle thickness increased by  $15.7 \pm 12.1\%$  ( $P = 0.050$ ). There were no significant differences between acute ( $< 12$  months) and chronic users of ADT for the outcome variables (data not shown).

### PSA, Serum Hormones, and Hemoglobin

After the 10- and 20-wk training period, there were no changes for PSA, free testosterone, GH, cortisol, or hemoglobin (Table 5). It should be noted that one subject (Table 1) initiated the study with a relatively high PSA level and experienced a subsequent drop in this marker during the intervention. Excluding this subject from the analyses resulted in PSA values of  $0.94 \pm 1.4$ ,  $0.92 \pm 1.2$ , and  $0.86 \pm 1.2$  ng·mL<sup>-1</sup> ( $P = 0.945$ ) at baseline, week 10, and week 20, respectively.

## DISCUSSION

This is the first study to comprehensively examine the effects of high-intensity progressive resistance training on muscle function, functional performance, balance, body composition, and muscle thickness in men receiving ADT for prostate cancer. Substantial improvements were seen in muscle strength, endurance, and thickness, and body composition and bone mass were preserved during the 20-wk intervention. Importantly, these changes were accompanied by enhancement in several measures of

functional performance and balance, with no change in PSA. These results suggest that high-intensity resistance exercise can be safely tolerated in this group of men receiving ADT and enhanced muscle and physical function ensues despite a compromised hormonal profile. These findings extend those reported by Segal et al. (16), who found an increased quality of life and decreased fatigue in men on ADT after 12 wk of resistance training, providing a rationale for why these benefits were observed.

In the present study, we found significant increases in muscle strength of 40–96%, which are comparable with the effects of this exercise mode in healthy older adults who are not on ADT (10). These observed changes are likely to be mediated by non-hypertrophy-related factors such as neural adaptations to resistance training, as previously described (15). We also assessed the effects of training on muscle endurance, an important neuromuscular parameter that has received only modest attention in exercise studies (11), and we observed considerable improvement for both the upper and lower body, especially when the baseline load was used during retesting. Similar enhancement of muscle endurance using a comparable exercise intervention in community-dwelling healthy older adults not on ADT has been previously reported (11), indicating that older adults, including those on ADT, may accomplish daily tasks more easily and with less fatigue after training. The combined results of increased muscle strength and endurance in the present study could partially explain the reduced levels of fatigue observed in the study by Segal et al. (16).

Changes in several functional performance measures were also observed in our cohort of men, and these changes are comparable with those of previous studies in healthy older adults undertaking resistance training (11,27). Our results are particularly important because they imply a greater reserve capacity. They also imply that daily activities can be more easily performed using a lower

TABLE 5. Prostate specific antigen (PSA), free testosterone, growth hormone (GH), cortisol, and hemoglobin at baseline and after 10 and 20 wk of resistance training (mean  $\pm$  SD).

	Baseline	Week 10	Week 20	P Value*
PSA (ng·mL <sup>-1</sup> )	3.09 $\pm$ 6.58	1.28 $\pm$ 1.58	0.90 $\pm$ 1.13	0.374
Free testosterone (pg·mL <sup>-1</sup> )	2.13 $\pm$ 3.64	2.15 $\pm$ 3.61	1.56 $\pm$ 3.68	0.532
GH (ng·mL <sup>-1</sup> )	0.72 $\pm$ 0.75	0.83 $\pm$ 0.78	0.48 $\pm$ 0.37	0.239
Cortisol (ng·mL <sup>-1</sup> )	10.63 $\pm$ 3.54	10.35 $\pm$ 3.32	10.42 $\pm$ 2.67	0.979
Hemoglobin (g·L <sup>-1</sup> )	141.3 $\pm$ 13.1	142.3 $\pm$ 14.4	141.2 $\pm$ 13.5	0.913

\* ANOVA (baseline, week 10, and week 20).

percentage of maximal strength and endurance, thereby promoting enhanced independence. In addition, balance was improved after training. The SOT equilibrium score has previously been used to discern fallers from nonfallers in healthy older adults (29). Skeletal fracture risk is now recognized as a major side effect from GnRH agonist treatment (17,22), and a relationship between the number of GnRH doses received during the initial 12 months after diagnosis and the subsequent risk for fracture has been reported (17). Our findings of improved functional performance and balance after an exercise program could markedly contribute to a reduction in falls and, hence, a reduced fracture risk during GnRH administration.

A large reduction in lean and bone mass and an increase in body fat are well-established side effects from ADT (6,12,14,17,19,22). Importantly, it has been suggested that these negative changes in soft tissue are more severe in the first 12 months of ADT (12). In the present study, whole-body LM, FM, and BMC, in addition to hip BMD, were preserved irrespective of acute or chronic ADT exposure. This is an important outcome because these well-known detrimental changes in the muscular and skeletal system are closely related to other chronic conditions (17,19,22) that can compromise independence and possibly affect mortality. In addition to whole-body soft tissue, we also examined local changes in skeletal muscle (targeted by the exercises) assessed by ultrasound. Interestingly, quadriceps thickness increased by 15% despite a severely reduced anabolic hormone environment.

Serum-free testosterone and PSA did not change during the study, indicating that this exercise mode can safely be undertaken in prostate cancer patients on ADT without compromising the therapeutic purpose of reduced androgen levels. The lack of change in testosterone and PSA is consistent with the only other published study in the area of resistance exercise and prostate cancer (16). Further, GH, which could mediate resistance training-induced adaptations, did not change as a result of the intervention. Additionally, we found that hemoglobin was also unaltered in our cohort, which may also provide a basis for Segal et al.'s (16) findings on reduced levels of fatigue after training. Anemia has been reported as one ADT-related side effect, with reductions in hemoglobin ranging from approxi-

mately 7 to 30% after therapy (20,21,25). The maintenance of hemoglobin levels in our group of men after 20 wk of exercise, as well as the enhancement in muscle strength and endurance, provides a likely mechanism for the prevention of fatigue in resistance-trained men on ADT.

Several limitations of the trial are worthy of comment. Although all subjects were undertaking ADT during the course of the study, duration of use varied. However, we found similar responses in training adaptations irrespective of acute or chronic ADT exposure, possibly because of the low number of subjects in the subanalysis. In addition, a randomized controlled trial would have been a stronger experimental design. However, it is likely that a control group after 6 months on ADT would have decreased in the study parameters and, as such, differences in the exercise group would seem even more substantial. It is important to point out that during the recruitment phase, all men reported that they would not have complied with a 20-wk control period if allocated to a control group, suggesting that future exercise trials should use alternative control exercise groups (e.g., cardiovascular, flexibility training) as a strategy to enhance long-term exercise study designs. Nevertheless, our study employed a comprehensive battery of measures to assess muscle and physical function, as well as balance, DXA, and compound ultrasound to study changes in soft tissue. Lastly, our subjects were well-functioning individuals who were mostly motivated to undertake the training program, and they may not be representative of all older men undertaking ADT for prostate cancer.

In summary, the present study indicates that resistance exercise has beneficial effects on muscle strength, functional performance, and balance in older men receiving ADT for prostate cancer and should be considered for preserving body composition and reducing musculoskeletal side effects. Randomized controlled trials are warranted to confirm these findings, and future studies should also include larger study groups, longer exercise periods (> 5 months), and training during intermittent regimens of ADT.

The authors thank Jesse Judge, MD, Joondalup Health Campus for assisting with patient recruitment. This research was supported by a Life Fitness Academy Michael Pollock Memorial Grant and Fitness Technology. D.G. has been supported by an Australian International Postgraduate Research Scholarship.

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