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TITLE: Exercise to Counteract Loss of Bone and Muscle During
Androgen Deprivation Therapy in Men with Prostate Cancer

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INTRODUCTION

The aim of the study is to determine whether a 1-year intensive resistance exercise training (RT) program is more effective than a moderate-intensity walking program in ameliorating the effects on body composition of androgen deprivation therapy (ADT). It is postulated that, in men on ADT for the treatment of locally advanced prostate cancer: 1) RT will attenuate the declines in bone mineral density (BMD) and fat-free mass (FFM) to a greater extent than walking; and 2) both RT and walking will prevent an increase in fat mass. A total of 40 men will be enrolled and randomized to either the RT or walking exercise programs. Primary outcomes are lumbar spine BMD and FFM. Secondary outcomes are: total body and hip BMD; fat mass; markers of bone turnover, to determine whether changes in BMD are the result of changes in bone resorption and/or formation; serum sex hormones, including testosterone, estradiol, estrone, and sex hormone binding globulin; physical functional performance; and quality of life. Local project support will enable additional assessments of risk factors for cardiovascular disease, including blood lipid profile, oral glucose tolerance, and arterial stiffness. These procedures were not included in the original grant application, but were described in the revised protocol that was approved by the local IRB and the HSRRB.

BODY

The tasks in the Statement of Work are as follows:

Task 1: Preparation to initiate studies; months 1 – 3

- secure local IRB and HSRRB approval for study
- apply for research support from the General Clinical Research Center (GCRC)
- apply for research support from the Clinical Nutrition Research Unit (CNRU)
- prepare data forms
- prepare data base
- train research staff

This task was completed. The local IRB initially approved the protocol on 31 December 2002. Thereafter, repeated interactions with the Army HSRRB resulted in numerous modifications to the protocol. The HSRRB-recommended changes were approved by the local IRB on 1 April 2004. Final approval of the protocol by the HSRRB was 8 August 2004. Thereafter, final approvals were obtained from the GCRC and CNRU for local project support. Recruiting efforts began in November 2004. The protocol underwent local IRB annual renewal in September 2004.

Task 2: Subject recruitment; months 4-21

- enroll 2-3 subjects per month, total of 40
- recruiting lectures at local prostate support group meetings
- meetings with private urology clinic staffs
- interactions with health reporters for local media
- place advertisements on newspaper and radio

Advertisements in Denver's two major daily papers, the Denver Post and Rocky Mountain News, were placed in November 2004. Also in November, the US TOO prostate cancer support group in Denver sent an email out to roughly 60 members and letters to 60 more men informing them of the study. We consented four participants in November. Of those four, the first was randomized in February. One of the remaining 3 dropped out prior to randomization due to time constraints and the others 2 participants did not qualify due to hypertension and initiation of bisphosphonate therapy, respectively. The PI gave a presentation to the UH urologic oncology clinic staff on the study in November 2004. The staff agreed to place study fliers in the clinic reception area.

In December, the PI presented to the US TOO prostate cancer support group. One man consented in December and did not qualify due to COPD. In January, ads were placed in the Aurora Sentinel and Mile High Guardian. The study was described in an article on aging and exercise that the PI wrote for the Glendale community newspaper in January. An email describing the study was circulated to the UCHSC community in January. No major recruitment were made in February because the study coordinator was out of town. In

March, the PI present to the American Cancer Society's Man-to-Man support group and the study coordinator presented to the support group at Lutheran Hospital in Wheatridge. Two men consented in March and one dropped after deciding he did not want to undergo any blood draws.

Protocol amendments were submitted to the local IRB in March to address the difficulty with recruitment. The age range of the study was expanded to 45-85 and the time restriction for initiation of ADT was eliminated to allow enrollment of men on intermittent ADT and men who have been on ADT for longer than 12 months. This criterion was in place because of the concern that long-term androgen deprivation lowers BMD and increases fracture risk. However, we have in place a screening test for BMD and men with severe osteopenia or osteoporosis (t scores below -2) must consult their primary care provider about possible need for treatment before they can be considered for eligibility. The original plan was to enroll only men on continuous therapy. However, intermittent therapy (timing of hormone injections based on rise in PSA) has become more popular. There is evidence that continuous and intermittent ADT are both associated with low BMD, so it seems unlikely that this modification detracts from the scientific aim to determine whether exercise can help preserve bone and muscle mass during ADT. The local IRB approved the modifications to the protocol and these changes are currently being reviewed by the HSRRB.

In April, brochures were sent to the entire Man-to-Man support group mailing list by the local chapter of the American Cancer Society. Also in April a radio ad was run over the course of a week on a local AM station. The study coordinator attend the 9 News Healthfair at a local church in April. Advertisements were place in the April issues of magazines at two large retirement communities (Windsor and Heather Gardens) in the Denver metro area. Five men were oriented to the study in April with 4 opting to consent.

In May, other members of the PI's research group attended the Salute to Seniors Event at the Denver Convention Center hosted by the Colorado Gerontological Society and distributed study fliers.

In summary, 38 men have inquired about the study, 12 provided informed consent, and we anticipate that 4 will be exercising by the end of the May 2005. Despite major efforts, recruitment has not met the projected rate of enrollment. We anticipate the rate of enrollment will improve if the suggested modifications to the enrollment criteria are approved. We will continue to recruit through the prostate support groups and place advertisements in media that have been successful in generating calls about the study. We will also explore the possibility of listing the protocol in the UCDHSC Cancer Institute's registry of clinical trials, which is accessible to medical and lay communities.

Task 3: Implement resistance exercise and walking exercise programs; months 5 - 32

- maintain records of attendance, exercise performance
- routine maintenance of equipment
- track progress of individual participants

This task is progressing as planned.

Task 4: Data acquisition and management; months 4 – 32

- schedule all baseline and follow-up testing sessions for all participants
- review all data forms prior to computerization
- enter data into database
- perform routine quality control of database
- track blood samples stored for batch analyses of sex hormones and markers of bone turnover to be performed as participants complete the intervention

This task is progressing as planned.

Task 5: Prepare schedule reports; months 1 to 36

- prepare required progress reports
- secure annual IRB (and HSRRB, if necessary) renewal of protocol
- file serious adverse event forms as necessary
- prepare abstracts for presentation

Annual IRB approval was obtained in September 2004. No serious adverse events have occurred.

KEY RESEARCH ACCOMPLISHMENTS

At this early stage of the project there are no key accomplishments.

REPORTABLE OUTCOMES

At the early stage of the project there are no reportable outcomes.

CONCLUSIONS

none

REFERENCES

none

APPENDICES

none