The Benefits of Exercise During Hormone Therapy

Hormone therapy, also known as androgen deprivation therapy (ADT), is a commonly used treatment for men with prostate cancer. ADT may serve as adjuvant therapy (administered after prostate removal or radiation therapy) or it may serve as primary therapy, as in the case of recurrent or metastatic prostate cancer to slow the advancement of the disease.

ADT works by reducing the body’s natural production of the hormone testosterone, slowing the progression of prostate cancer cells that are dependent on testosterone for growth. While ADT improves cancer-related symptoms and survival, testosterone deprivation has numerous side effects that may have negative consequences for overall health and quality of life. Exercise has been proposed as a strategy to counter the adverse effects of ADT and is already considered to be an effective treatment for chronic diseases such as type II diabetes and cardiovascular disease. Many men treated with ADT recognize the importance of doing exercise to stay healthy; however, the exact exercise prescription may be less clear. The focus of this article will be to discuss how exercise may help with treatment-related effects, and what types of exercise may be most effective.

Body Composition and Exercise

A primary side effect of ADT is the loss of muscle and increase in body fat within 3 to 12 months of starting treatment [1]. Muscle loss reduces strength, increasing frailty, and interferes with activities of daily living. Together, the loss of muscle and gain of fat—termed sarcopenic obesity—contribute to insulin resistance and greater risk of diabetes. Numerous studies have explored how exercise might be used to counter ADT-related sarcopenic obesity and its long-term effects. Prevention of muscle loss was observed with exercise programs that were at least 3 months long and involved resistance exercise rather than aerobic exercise [2-4]. Resistance exercise utilizes weights, either machines or free weights, while aerobic exercise elevates heart rate for an extended period of time, such as walking, cycling, or swimming.

Our current work at the University of Southern California investigates how resistance exercise, either alone or combined with whey protein supplementation, can actually increase muscle mass in men receiving ADT, not just simply maintaining it [5]. Our preliminary results suggest that ideally, weight exercises should be done 3 times per week targeting major muscle groups, beginning at a moderate intensity and progressing weekly to a vigorous intensity, with limited rest periods. For example, a chest press exercise, which involves more muscle mass, is preferred over a biceps curl exercise. Furthermore, instead of the same weight for the entire program, the exercises should start at light weight and high repetitions (>12) and slowly progress throughout the weeks to heavier weight and less repetitions (~8). Finally, minimal rest (< 60 seconds) should be taken between sets as a
way of keeping the heart rate elevated in a manner similar to aerobic training.

There is less evidence for the effectiveness of exercise in reducing fat mass during ADT. In one study, men who performed aerobic exercise or who did not exercise, experienced body fat gains, while those on weights exercise did not [4]. However, other studies have shown no effect of weights exercise on fat mass [3, 6]. Since other factors, such as diet, ADT duration, and age likely influence changes in fat, more research is needed in this area to clarify the role of exercise in fat loss for men on ADT.

**Physical Function**

ADT-related muscle loss can lead to poorer performance on physical tasks, increasing the risk of fracture, falls, and difficulty with independent living. In one study, prostate cancer patients on ADT had reduced muscular strength and slower walking speeds compared to men of the same age who were cancer-free [7]. Many studies have found weights exercise to be beneficial in increasing muscular strength during ADT when the exercise is performed at least twice per week for 3 months [3, 4, 8]. In addition, weights exercise was found to improve functional tasks like standing up after sitting [8], although not stair climbing or balance [3]. These studies lend insight into the nature of adaptations to exercise; adaptations are specific to the movement trained. General resistance exercise using machines and weights are useful at increasing strength, but do not necessarily translate to better functional performance. In other words, to improve balance, one must do balance exercises in addition to strengthening the leg muscles. Some exercises can double as both functional and strengthening movements, such as the split squat, where one stands with one foot forward and one foot behind, and bends and straightens the legs. We use exercises such as the split squat for men on ADT to improve strength, balance, and mobility.

**Fatigue**

A universal side effect reported by patients on ADT is fatigue, which may be attributed to any number of ADT-related complications including loss of muscle, low red blood cells, distressed emotional state, or disruption of sleep [9]. Several studies have observed significant reductions in fatigue as a result of exercise training, be it resistance or aerobic [4, 8, 10]. In particular, performing either aerobic or resistance exercise at least twice per week reduced fatigue compared to not exercising at all.

**Quality of Life**

The impact of ADT on emotional state is substantial, with depressed mood and increased anxiety documented across several studies in men receiving ADT [11-13]. Long-term use of ADT and the presence of other disease was associated with poorer quality of life, while men who remained physically active had greater psychosocial well-being [13]. Indeed, many studies have demonstrated that men on ADT have a more positive outlook after participating in an exercise program compared to those who did not exercise [3, 4, 10, 14]. This greater well-being may be due to improvements in muscle strength and body composi-
tion, although the social aspect of being involved in a fitness program is also a possible factor.

Anecdotally, we have found that patients who complete our intervention have enjoyed participating in a community of exercisers and trainers as much as doing the exercises themselves. In fact, many participants finish our study on a first-name-basis with other participants whom they see every week. In addition, the exercise trainers become part of the support network for patients; through their encouragement and feedback, participants improved in their movements. This self-efficacy is often carried beyond the walls of our laboratory to work, leisure activities, or tasks of daily living. The concept of exercising with a partner is the premise behind community-based wellness classes for cancer survivors, such as the weekly class at the USC Norris Comprehensive Cancer Center.

Participants are encouraged to bring a family member or friend, strengthening the bond between the patient and their partner as they exercise together.

Conclusions

More men with prostate cancer on ADT are recognizing that treatment for cancer extends beyond the doctor’s office, and that exercise may be effective in managing certain aspects of the disease. A growing body of research supports the use of exercise during treatment with ADT, as exercise, particularly resistance exercise of major muscle groups, appears to lessen some ADT-related side effects. When prescribed and performed correctly, the potential benefits of exercise range from improving muscle mass and physical performance to increasing quality of life. Ideally, exercising as part of a community, either by working with a qualified trainer, taking a class with a partner, or participating in a research study with exercise, will enhance the psychosocial benefit. Men on hormone therapy interested in starting an exercise regimen should discuss with their doctor the type of exercise that would be most appropriate.

Prostate Cancer & Exercise Research

The Clinical Exercise Research Center at USC is conducting a study about improving the health in men being treated for prostate cancer. We hope to learn about how resistance exercise and protein supplementation can increase muscle mass, strength, and physical function. (USC IRB #HS–13–00315)

For more information and how you can participate, contact Jackie Kiwata, MS at kiwata@usc.edu, 323.442.2180 or visit pt.usc.edu/ProstateCancerResearch

Exercise Do’s and Don’ts

<table>
<thead>
<tr>
<th>Do</th>
<th>Don’t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform regular exercise incorporating aerobic and resistance training 2-3x/week</td>
<td>Avoid regular physical activity</td>
</tr>
<tr>
<td>Resistance exercise should focus on large muscle groups (e.g. chest press, lat pulldown, leg press, leg curl) combined with dynamic movements (e.g. split squat, forward lunge)</td>
<td>Perform only single joint exercises (e.g. using only exercise machines)</td>
</tr>
<tr>
<td>Exercise with someone (e.g. a trainer, workout partner, or family member)</td>
<td>Continue to use light weights (even as the movements become easier with training)</td>
</tr>
<tr>
<td>Discuss starting any rigorous exercise program with your physician</td>
<td></td>
</tr>
</tbody>
</table>

- **Mitchell Gross, MD** is the Research Director of the USC Westside Cancer Center and the Center for Applied Molecular Medicine and Associate Professor of Medicine and Urology at the USC Keck School of Medicine.
- **Tanya Dorff, MD** is an Assistant Professor of Medicine at the USC Keck School of Medicine.
- **E. Todd Schroeder, PhD** is an Associate Professor and Director of the Clinical Exercise Research Center at USC.
- **Jackie Kiwata, MS** is a doctoral student under Dr. Schroeder who leads the study “Exercise and Whey Protein Supplementation for Men with Prostate Cancer on ADT,” which is currently ongoing at USC.