

# Exercise training in prostate cancer patients on androgen deprivation therapy

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## Summary

Androgen deprivation therapy (ADT) forms the cornerstone in the treatment of advanced prostate cancer (PCa). By suppressing testosterone to castration levels, tumor progression is inhibited. However, ADT also results in adverse effects like a decrease in muscle mass and an increase in fat mass. In **chapter 2**, we elucidate on the working mechanism of ADT during prostate cancer, and its adverse effects on skeletal muscle mass. In addition, resistance exercise training is introduced as potential strategy to combat these adverse effects, including an overview of the literature on this topic. In chapter 3 to chapter 6, we describe the results of our studies on the effects of resistance exercise training, with or without protein supplementation, during ADT. In **chapter 3**, we first assessed the adverse effects of ADT. Initiation of ADT results in increases in body fat mass and insulin levels, and decreases in skeletal muscle mass, muscle strength, aerobic capacity, physical activity and health-related quality of life. In **chapter 4**, the effect of resistance exercise training on these adverse effects is examined. A supervised resistance exercise program of 20 weeks not only preserved, but even increased muscle mass and strength. Furthermore, resistance exercise training attenuated the increase in fat mass and the decline in aerobic capacity. In addition, we examined whether protein supplementation could enhance the effect of the resistance exercise training. We found no additional effect of the protein supplementation, probably because habitual protein intake in our population was already sufficient (>1.0 g per kg body weight per day). In **chapter 5**, we zoomed in on the effects of ADT and resistance exercise training on skeletal muscle fiber characteristics. We found that ADT results in a decrease in type I and type II-muscle fiber size and capillarization. Resistance exercise training, counteracted this decrease and resulted in an increase in type I and type II muscle fiber size and type I muscle fiber capillarization. In **chapter 6**, we examined whether the exercise-obtained benefits were preserved on the long term. For that, we reassessed outcome measures 1 year after study enrollment - about 7 months after cessation of the supervised exercise training intervention. Despite the high percentage of patients (83%) reporting exercise continuation, the obtained effects following supervised exercise training were not well preserved. After 1 year, no differences in fat percentage and muscle mass were found between the former exercise training and control group. For fat mass and muscle strength, still some differences existed in favor of the former exercise trained group.

In **chapter 7**, we shift our focus to exercise training as potential strategy to attenuate tumor progression. For that, we requested prostate cancer patients scheduled for a radical prostatectomy, to pursue a low or high daily step count in the week before surgery. No differences in tissue protein synthesis rates of prostate tumor, healthy prostate, or skeletal muscle tissue were found between the groups with the low and high daily step count. Probably our intervention was either not intense, or not long enough. We did find that the tissue protein synthesis rates were almost twofold higher in prostate tumor tissue when compared to the surrounding healthy prostate tissue.

We conclude this thesis with a discussion about the implications of our study results for clinical practice (**chapter 8**). Given the proven effectivity of resistance exercise training during ADT, we advocate implementation of resistance exercise training as part of the standard prostate cancer care. Therefore, we give advises regarding the training program, discuss challenges, and give suggestions for further research.