

RESEARCH ARTICLE

Prehabilitation: The effectiveness of exercising prior to prostate cancer surgery.

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Abstract

Prostatectomy is associated with short- and long-term morbidity, which includes attenuation of cardiovascular and muscle function, as well as the deterioration of lean body mass. Physical function is a known predictor of morbidity and mortality, with initial evidence indicating that pre-surgical exercise is associated with fewer post-surgical complications and shorter hospitalisation. Prehabilitation has been previously shown to be more effective in enhancing postoperative functional capacity than rehabilitation alone. Evidence grows indicating benefits to clinical, physical and quality of life outcomes. Exercising within this critical period between cancer diagnosis and surgery allows the usage of surgical wait time to promote and facilitate health behaviour changes that can lead to altering prostate cancer patient management. By combining exercise with a nutritional and psychological intervention a prostate cancer patient can be set up to significantly improve preoperative physical and mental fitness in preparation for surgery and beyond.

Key words: Prostate cancer, Exercise, Surgery, Prehabilitation, Prostatectomy, Pre-surgery, Post-operative recovery, Post-operative complications.

Introduction

Prostate cancer (PCa), is a commonly diagnosed cancer in men.¹ Prostatectomy, the primary curative treatment for localised disease, has a 5-year survival rate of ~90%.² However, it is associated with adverse effects including incontinence and reduced physical function³ that negatively impact quality of life.⁴ An analysis of over 100,000 patients indicated that major complications following surgery occur in 19.3% of cases and was shown to extend the length of hospital stay, increase readmissions and elevate costs, negatively influencing patient function and having lasting consequences on mortality.⁵ Severe complications are associated with substantial increases in costs when compared to non-complicated surgeries⁶ and any significant complications within 30-days post-surgery reduce survivorship by 69%.⁵ The elderly and those that fall into the high-risk populations, are more susceptible to the damaging effects of surgical stress and can be so significantly afflicted that they may not regain their baseline functioning. A lower or reduced level of prior surgery physical fitness levels and status are significant risk factors for life-threatening postoperative complications and long-term disability.⁷

Exercise and Prehabilitation

Any movement effectively acquiring a metabolic cost above rest is defined as “physical activity”, while “exercise” refers to a specified and prescribed session of physical activity done routinely with a purpose to derive substantial health benefits.⁸ Exercise has shown to have a positive outcome in attenuating treatment-related adverse effects and is currently recommended by professional exercise health organisations⁹⁻¹² to enhance cardiovascular and musculoskeletal function in cancer survivors. The long term benefits of exercise are

evident, with research suggesting that even modest increments in physical activity of 1 MET (metabolic equivalent) is associated with a reduction in mortality by about 20%.¹³ There is a 52% increase in all-cause mortality, a twofold increase in cardiovascular-related mortality and a 29% increase in cancer-related mortality as described by Hu et al.¹⁴ for physically inactive middle age women when compared to their physical active counterparts. Furthermore, a large and extensive clinical evidence now clearly and succinctly indicates that exercise can effectively ameliorate adverse physical and psychosocial effects of some cancers (breast, prostate, lung, colorectal) and their specifically related treatments.¹⁵⁻²⁰ Regular physical activity and exercise does have significant health benefits and lowers the risk of death for many disease.²¹

Traditionally, exercise interventions to reduce adverse effects from prostatectomy were limited to the post-surgical period or as rehabilitation with exercise protocols focusing on pelvic floor muscle exercises (PFME).²² Although post-surgical incontinence incidences have reduced, it is still a troublesome affliction.^{23,24} Moreover, the decline of physical function in this period is particularly detrimental given the age of the men and potentially low physical reserve capacity. Physical functioning, one- and three-months post-surgery are below population norms.^{25,26} A more opportune time to intervene with exercise may be the pre-surgical period to negate or attenuate the treatment-related adverse effects thereby aiding recovery from surgery, and enhancing short- and long-term patient outcomes.²⁷ Improving physical reserve capacity at this early stage can be akin to an individual training for a physical challenge, prehabilitation, as suggested by Carli et al.²⁷, can be a game-changing strategy to improve

and tackle specific adaptable risk factors which can positively alter post-surgical cancer treatment outcomes. Despite the viable opportunity, a patient's genetics and innate physiological, psychological and social capabilities may pose limitations to their exercise response capacity. This is further compounded by the short and inadequate time between diagnosis and treatment.²⁸

Early evidence suggests that exercise before a range of different surgeries (mastectomy, lung, abdominal) is associated with fewer post-surgical complications and shorter hospitalisation²⁹⁻³³, leading to improved health outcomes and reduced health care costs.^{34,35} Many of these interventions employed either systemic (general) exercise focused on addressing musculoskeletal/cardiovascular deconditioning and/or more specific specialised training targeting the tissue level (therapeutic). Therapeutic training can include pelvic floor exercises for prostate patients or breathing and diaphragmatic exercises for lung surgery patients, all depending on the type of disease condition and the treatment-related morbidity.⁸ The systematic review by Santa Mina et al.³⁶, focusing on total body exercise done during prehabilitation found consistent improvements in physical function; with contrasting outcomes for other physical and psychosocial symptoms for the control patients that did not exercise. Patients that exercise during the preoperative period, had superior and faster returns to baseline physical function levels, higher pain thresholds and shorter hospital stay compared to the control subjects.

Within the cancer continuum, as defined by Courneya and Friedenreich³⁷, prehabilitation forms the initial part occurring during the pre-treatment phase

between the time of diagnosis and the start of acute oncological treatment. Cancer prehabilitation as defined by Silver et al.³⁵ is "A process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments". Several oncological studies have now shown within this opportunistic period effective management of treatment related adverse effects and improved aerobic and functional capacity outcomes.^{31,38-40} A review paper found that exercise training had resulted in statistically significant increases in peak VO_2 in cancer patients (haematological, breast, prostate and colon) after conducting a meta-analysis with pooled data from six cancer randomized controlled trials.³⁸ Using different modality, other studies demonstrated positive outcomes in physical functional capacity indicated by difference assessments such as 6-min walk test^{39,40} and aerobic capacity.³¹ The feasibility of exercising during neoadjuvant therapy before surgery has been explored by Singh et al.⁴¹ and West et al.³¹, demonstrated the effectiveness of prehabilitation to significantly prevent or attenuate the loss of physical functional capacity caused by neoadjuvant therapy prior to major rectal surgery.

To date, the role of exercise prior to prostatectomy has centred on PFME to reduce incontinence. An international review and meta-analysis of prehabilitation studies in cancer compared to usual care was done by Treanor and colleagues in 2018.⁴² Extracting only prostate cancer studies, the review described four studies investigating the comparable effects of PFME and usual care

on continence related outcome, lifestyle and functional ability and satisfaction. Urinary continence meta-analysis indicated that those performing PFME significantly more likely to recover at 3 months post-surgery (OR = 3.29, 95% CI = 1.57-6.91, I2 = 15%). The review also described each component of the individual studies and many of the outcomes indicated a favourable urinary continence outcome for the intervention group at different time points post-surgery. Results support PFME training prior to prostatectomy⁴³⁻⁴⁵, but, this method does not address other adverse effects such as the loss of muscle mass and reduction in physical function that accompanies surgery and the post-surgical period. Indeed, the decline in muscle mass and physical function may be quite problematic for those men with poor physical function prior to surgery.

Currently, there have been two published studies on this novel area of 'prehabilitation' and PCa focusing on increasing muscle mass, physical function and recovery. The initial paper was a preliminary feasibility study⁴⁶, with the primary objective to facilitate many of the described outcomes. Recruiting and assessing ten PCa patients with 6 weeks of supervised aerobic and resistance exercise training above their normal usual care prior to surgery, showed that patients increased and improved strength and physical function from baseline. Following surgery, assessments found many of these improvements in physical performance were maintained, with some having better results when compared to baseline levels. Presurgical exercise was feasible to potentially facilitate recovery by improving physical reserve capacity for sedentary men. The second study a recently published randomised controlled trial in prehabilitation and PCa⁴⁷, focused on a home-based exercise intervention program. The prehabilitation

group received home-based, moderate-intensity exercise prior to surgery with the control group receiving the usual care conditions. Results indicated that the prehabilitation group demonstrated less anxiety and a reduced body fat percentage before surgery with better physical function scores after surgery. The attrition rates were lower for the prehab group compared to the controls, with the authors concluding that a program done before surgery does have promising benefits to both physical and psychological wellbeing.

The effect of an exercise intervention prior to surgery on improving the deleterious cancer treatment-related adverse effects can provide immediate and lifelong benefits with the potential to contribute to a better overall patient pre-surgical medical management by altering previously out-dated methods of usual care. A urologist may be able to consider a pre-surgical exercise intervention as a potential neoadjuvant therapy to improve PCa patient post-surgical outcomes. Cancer 'prehabilitation' is now gaining noteworthy acceptance as part of the cancer care continuum provide cancer survivors with the best medical care to improve recovery and health care cost. PCa patients can now consider this relatively simple and cost-effective intervention, which may provide some incentive in terms of accelerating the return to normal daily activities. In terms of medical cost, the annual economic burden to promote survivorship from cancer was \$16,213 per person aged 18-64 years and \$16,441 per person aged 65 years and older⁴⁸ and the direct cancer-related annual medical costs range between \$25.2-41.7 billion and \$37.3-48.1 billion, respectively.⁴⁸ Moreover, readmission rates after all major cancer surgery including prostatectomy were between 16-25% at 30 days and 52-66% at 1 year.⁴⁹ Furthermore, those that are readmitted tend to have poorer survival outcomes.^{50,51}

Lengthy bouts of hospitalisation cause an increase of treatment cost, hospital resources and bed cost. A reduction of 0.5 days in the length of hospital stay can save an estimate \$457-\$846 in hospital cost.⁵² As the prevalence of living with PCa is increasing, interventions that can immediately improve health for PCa patients are of critical importance. Improving recovery periods can significantly reduce the dependence on pharmaceutical interventions, hospitalisation time, readmission rates, and overall healthcare costs.

Exercise does have many significant benefits for a prostate cancer patient when prescribed and structured in accordance with the needs and goals of the client. It is just one of the many prescribed “medications” that is required for health maintenance, improvement and enhancement. Other “medications” to improve health outcomes for patients are modalities such as nutritional⁵³ and psychological⁵⁴ interventions. These interventions can either work alone or in combination with exercise^{55,56} to further improve, maintain or enhance patients’ health outcome. Carli et al.²⁷ described prehabilitation as not a “one size fits all” program and suggested that such programming requires detailed assessments of individuals and specific interventions for

patient’s health improvements. Therefore, including these interventions together with exercise before prostatectomy can further enhance patient’s health outcomes and most importantly recovery following surgery.

Conclusion

Current recommended rehabilitation management strategies are relatively poor and if left unmanaged, these adverse effects can cause a negative spiral in physical and mental function. Translation of the findings that place a greater emphasis on pre-surgical fitness could result in lifelong benefits improving not only surgical recovery and accelerating the return to normal daily activities, but also providing the tools for leading a healthy lifestyle. Improving the post-surgical recovery period has the potential to reduce dependence on pharmaceutical interventions, hospitalisation time, and overall costs.³⁴ Exercise as a form of medical therapy that will not only lead to altering PCa patient management but also has the potential to provide vital information during this critical window of opportunity for improving patient health outcomes, increasing cancer survivability and reducing cancer manifestation.

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