Cancer patients with bone metastases have previously been excluded from participation in physical activity programmes due to concerns of skeletal fractures. Our aim was to provide initial information on the association between physical activity levels and physical and mental health outcomes in prostate cancer patients with bone metastases. Between 2012 and 2015, 55 prostate cancer patients (mean age 69.7 ± 8.3; BMI 28.6 ± 4.0) with bone metastases (58.2% >2 regions affected) undertook assessments for self-reported physical activity, physical and mental health outcomes (SF-36), objective physical performance measures and body composition by DXA. Sixteen men (29%) met the current aerobic exercise guidelines for cancer survivors, while 39 (71%) reported lower aerobic exercise levels. Men not meeting aerobic exercise guidelines had lower physical functioning ($p = .004$), role functioning (physical and emotional) ($p < .05$), general health scores ($p = .014$) as well as all lower measures of physical performance ($p < .05$). Lower levels of aerobic exercise are associated with reduced physical and mental health outcomes in prostate cancer patients with bone metastases. While previous research has focused primarily in those with non-metastatic disease, our initial results suggest that higher levels of aerobic exercise may preserve physical and mental health outcomes in prostate cancer patients with bone metastases.

**KEYWORDS**

Exercise, Prostate Cancer, Bone Metastases, Physical Function, Quality of Life

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**INTRODUCTION**

Approximately, 80% of men with advanced prostate cancer are affected by bone metastatic disease (Small, Smith, Seaman, Petrone, & Kowalski, 2003). The disease itself as well as the long-term medical treatment cause extensive adverse effects which have a profound impact on patient’s physical function and quality of life (Saad, Olsson, & Schulman, 2004). Skeletal metastases result in significant complications such as bone pain, impaired mobility, symptomatic hypercalcemia, pathological fractures and spinal cord compression (Carlin &
Andriole, 2000; Coleman, 2001). Furthermore, long-term androgen deprivation therapy, which is usually administered to these patients, reduces bone mineral density, muscle mass/strength and physical functioning (Galvao et al., 2008, 2009; Smith, 2004; Wall et al., 2015). Functional impairments and muscle atrophy increase the risk of falls, which is accompanied by an increased risk of fracture due to treatment-related bone loss and bone metastases/skeletal-related events (Shahinian, Kuo, Freeman, & Goodwin, 2005). Although bone metastatic prostate cancer remains incurable, advances in medical treatment have prolonged the clinical course of the disease (5-year survival rate 46%) (Coleman, 2001). Consequently, reducing the burden of the disease by improving physical function and quality of life could provide clinically meaningful benefits to patients. It is therefore important to identify supportive measures that can be offered to these patients to address disease and treatment-related adverse effects to improve physical and mental health outcomes.

Over the last few years, clinical trials have consistently demonstrated the beneficial effects of exercise in prostate cancer survivors, counteracting a number of treatment-related side effects and improving quality of life (Baumann, Zopf, & Bloch, 2012; Bourke et al., 2016; Galvao, Taaffe, Spry, & Newton, 2007; Schmitz et al., 2010). Furthermore, regular physical activity has been associated with a 61% reduction in prostate cancer death (Kenfield, Stampfer, Giovannucci, & Chan, 2011). Although, to date, patients with bone metastases have been almost always excluded from exercise trials due to the concerns of skeletal fractures, current guidelines on exercise prescription for cancer survivors recommend that even patients with advanced bone metastatic disease should avoid inactivity (Schmitz et al., 2010). However, whether higher physical activity levels are associated with better physical and mental health outcomes in men with bone metastatic prostate cancer is unknown.

The aim of this preliminary study was to examine associations between physical activity levels and physical and mental health outcomes in prostate cancer patients with bone metastases and in particular to explore the difference between those patients meeting the current aerobic exercise guidelines for cancer patients and those who are less active. We hypothesised that due to functional impairments and concerns of fragility fracture, prostate cancer patients with bone metastases would have low levels of physical activity and that lower levels of activity would be associated with poorer physical and mental health outcomes.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

Prostate cancer patients were referred by their oncologists and urologists in Perth, Western Australia from August 2012 through August 2015. Patients were recruited as part of a randomised controlled trial that is ongoing (Galvao et al., 2011), with cross-sectional baseline data reported in this paper. Patients were eligible if they had established bone metastases according to their most recent bone scan, were able to read and speak English, did not have an acute illness, significant bone pain, or musculoskeletal or cardiovascular or neurological disorders that could inhibit or put them at risk from exercising and were not already undertaking structured and supervised aerobic and/or resistance training two or more times per week within the past 3 months. The study was approved by the Edith Cowan University Human Research Ethics Committee and all participants provided written informed consent.

2.2 | Outcome measures

2.2.1 | Physical activity

Self-reported physical activity levels were measured with the Modified Godin Leisure-Time Exercise Questionnaire, which assesses the average frequency and duration of mild, moderate, vigorous and resistance exercise during free time in a typical week in the past month (Godin & Shephard, 1985). Mild exercise is defined as activity that requires minimal effort, such as fishing, golf and easy walking. Moderate exercise is described as activity that is not exhausting such as running, jogging, football, vigorous swimming and vigorous cycling. According to the recommendations of the American College of Sports Medicine and the American Cancer Society, patients had to perform at least 150 min of moderate intensity or 75 min of vigorous (or a combination of moderate and vigorous) aerobic exercise per week to meet the current aerobic exercise guidelines for people with cancer (Schmitz et al., 2010). To determine the percentage of patients meeting aerobic exercise guidelines, we calculated “exercise minutes” as minutes of moderate exercise plus two times minutes of vigorous exercise per week. The variable “exercise minutes” was also used to perform correlations.

2.2.2 | Quality of life

Quality of life was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). The questionnaire was used to assess patient-rated physical and mental health outcomes across the following domains: physical function, role function (physical and emotional), body pain, general health, vitality, social function and mental health. The eight domains add up to two sum scores, a physical component summary score and a mental component summary score (Ware & Sherbourne, 1992).

2.2.3 | Physical performance, body size/composition and prostate-specific antigen

Given that the reduction of lean mass following prostate cancer treatments can impact musculoskeletal fitness, compromising muscle strength, physical function and physical reserve capacity, we implemented a number of objective measures of physical function as part of our study. These were assessed by means of the 400-m walk, the 6-m walk (usual and fast pace), and the timed up and go test (Galvao et al., 2011). Participants with proximal femur bone lesion were excluded.
The 6-m walk and the timed up-and-go test were performed three times by each patient and the best performance was used in the analyses. Additionally, hip and waist circumferences were recorded and whole body fat and lean mass assessed by dual-energy X-ray absorptiometry (Hologic Discovery A, Waltham, MA). Prostate-specific antigen (PSA) levels were measured commercially by an accredited Australian National Association of Testing Authorities Laboratory (Pathwest Diagnostics, Perth, WA).

### 2.3 Statistical methods

Data were analysed using IBM SPSS statistics for windows, version 21.0. The Shapiro–Wilk test was used to assess normality of the data. Descriptive statistics and frequency tables were calculated to describe the activity levels of the screened patients and to depict the percentage of patients meeting the current aerobic exercise guidelines for cancer survivors. Spearman’s rank-order correlation was used to assess associations between exercise minutes (which were not normally distributed) and physical and mental health outcomes for all patients. Independent Student t-tests or non-parametric Mann–Whitney U-tests, as appropriate, were performed to compare the group of patients meeting the aerobic exercise guidelines to the group of patients not meeting the aerobic exercise guidelines with regard to their health outcomes. Contingency table and chi-square statistics were used to analyse categorical variables. p < .05 are considered significant.
TABLE 2 Spearman’s rank correlation coefficients of exercise minutes and physical and mental health outcomes

<table>
<thead>
<tr>
<th>Exercise minutes</th>
<th>Physical Functioning</th>
<th>Role functioning-physical</th>
<th>Bodily pain</th>
<th>General health</th>
<th>Vitality</th>
<th>Social functioning</th>
<th>Role functioning-emotional</th>
<th>Mental health</th>
<th>Physical component summary</th>
<th>Mental component summary</th>
<th>Usual pace 6-m walk (s)</th>
<th>Fast pace 6-m walk (s)</th>
<th>400-m walk (s)</th>
<th>Timed up and go (s)</th>
<th>Waist circumference (cm)</th>
<th>Hip circumference (cm)</th>
<th>Whole body lean mass (kg)</th>
<th>Whole body fat mass (kg)</th>
<th>Whole body fat mass (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.453**</td>
<td>0.318*</td>
<td>0.174</td>
<td>0.425**</td>
<td>0.226</td>
<td>0.283*</td>
<td>0.213</td>
<td>0.222</td>
<td>0.383**</td>
<td>0.177</td>
<td>−0.338*</td>
<td>−0.337*</td>
<td>−0.400*</td>
<td>−0.349*</td>
<td>−0.136</td>
<td>−0.259</td>
<td>0.080</td>
<td>−0.222</td>
<td>−0.320*</td>
</tr>
</tbody>
</table>

*Correlation is significant at the .05 level (two-tailed).
**Correlation is significant at the .01 level (two-tailed).

3 | RESULTS

3.1 | Participant characteristics

A total of 103 patients with prostate bone metastatic disease were screened for participation in a 3-month exercise trial (Galvao et al., 2011). Forty-six patients declined participation or were excluded for the following main reasons: declined/self-reported too unwell to participate (n = 16), too far to travel (n = 9), no time for training (n = 6), significant bone pain (n = 5), declined practitioner/physician consent (n = 5), no bone metastases (n = 1), unable to be contacted (n = 3), and already undertaking structured aerobic or resistance training (n = 1). In this report, we present the results from baseline assessment of all eligible patients (n = 55) who undertook complete physical activity assessment data at baseline. Patient characteristics are presented in Table 1. On average patients were 69.8 years of age with a BMI of 28.6. The majority of patients (58.2%) had more than two bone regions affected by bone metastases. There were no significant differences in participant characteristics between men not meeting aerobic exercise guidelines (n = 39) and those meeting guidelines (n = 16).

3.2 | Moderate and vigorous exercise participation

For minutes of moderate and vigorous exercise, 42% of patients had 0 min, 9% of patients achieved 1–49 min, 20% of patients achieved 50–149 min, and 29% of patients achieved ≥150 min.

3.3 | Correlations between aerobic exercise and physical and mental health outcomes

When correlating exercise minutes (moderate + vigorous) with physical and mental health outcomes based on the SF-36 and objective measures, significant associations between patients’ physical activity levels and the following outcomes were observed: physical functioning (rc = .453, p = .001), role functioning-physical (rc = .318, p = .018), general health (rc = .25, p = .001), social functioning (rc = .283, p = .036), physical component summary (rc = .383, p = .004), usual pace 6-m walk (rc = −.338, p = .012), fast pace 6-m walk (rc = −.337, p = .001), 400-m walk (rc = −.400, p = .021), timed up and go test (rc = −.349, p = .048) and whole body per cent fat (rc = −.320, p = .018) (Table 2).

3.4 | Compliance with aerobic exercise guidelines and association with physical and mental health outcomes

Only 16 men (29%) met the current aerobic exercise guidelines for cancer survivors (≥150 min of moderate intensity or ≥75 min of vigorous exercise per week or an equivalent combination), while 39 (71%) were insufficiently active (not meeting recommendations). Men who were not meeting the aerobic exercise guidelines had significantly lower physical functioning (p = .004), role functioning (physical and emotional) (p < .05) and general health scores (p = .014) than men who met the guidelines, resulting in a lower physical component summary score (p = .010) in the SF-36 questionnaire (Table 3). There were no significant differences in bodily pain between the groups. Regarding the objective physical health outcomes, patients that were not meeting aerobic exercise guidelines for cancer survivors had significantly slower 6-m walk (usual and face pace) and 400-m walk times (p < .05) compared to those men meeting the guidelines, indicating reduced physical performance. The waist circumference, hip circumference and percentage whole body fat mass was also significantly higher (p < .05) in the patient group not meeting aerobic exercise guidelines (Table 4).

4 | DISCUSSION

A number of studies have consistently demonstrated the beneficial effects of exercise in prostate cancer patients with localised disease (Galvao et al., 2007; Baumann et al., 2012; Schmitz et al., 2010). In this report, we extend this work to patients with advanced bone metastatic disease by showing significant associations between levels of aerobic exercise and selected health outcomes, with those with higher levels of aerobic exercise having greater physical and mental health scores. While previous research has focused primarily on non-metastatic cancer patients, our initial results suggest that meeting aerobic exercise guidelines may have clinically meaningful benefits for prostate cancer patients with advanced bone metastatic disease by preserving health outcomes. In particular, we observed better self-rated physical functioning, role functioning (physical and emotional), and general health. Patients who met the aerobic exercise guidelines...
TABLE 3 Quality of life outcomes (SF-36) and group differences with respect to meeting and not meeting the aerobic exercise guidelines

<table>
<thead>
<tr>
<th></th>
<th>Not meeting aerobic exercise guidelines (n = 39)</th>
<th>Meeting aerobic exercise guidelines (n = 16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning [median (IQR)]</td>
<td>46.5 (38.1–50.7)</td>
<td>52.8 (50.7–54.4)</td>
<td>.004a</td>
</tr>
<tr>
<td>Role functioning-physical [median (IQR)]</td>
<td>39.7 (29.9–49.5)</td>
<td>49.5 (40.9–56.9)</td>
<td>.021a</td>
</tr>
<tr>
<td>Bodily pain [median (IQR)]</td>
<td>51.1 (46.1–55.4)</td>
<td>55.4 (52.2–62.1)</td>
<td>.056</td>
</tr>
<tr>
<td>General health (mean ± SD)</td>
<td>39.4 ± 9.8</td>
<td>47.5 ± 9.6</td>
<td>.014a</td>
</tr>
<tr>
<td>Vitality (mean ± SD)</td>
<td>48.0 ± 11.4</td>
<td>53.7 ± 8.5</td>
<td>.116</td>
</tr>
<tr>
<td>Social functioning [median (IQR)]</td>
<td>39.4 (30.7–48.1)</td>
<td>48.1 (40.5–48.1)</td>
<td>.059</td>
</tr>
<tr>
<td>Role functioning-emotional [median (IQR)]</td>
<td>40.3 (31.0–46.5)</td>
<td>46.5 (41.1–46.5)</td>
<td>.024a</td>
</tr>
<tr>
<td>Mental health [median ± SD]</td>
<td>49.5 ± 10.6</td>
<td>55.1 ± 7.6</td>
<td>.072</td>
</tr>
<tr>
<td>Mental component summary (mean ± SD)</td>
<td>44.3 ± 8.8</td>
<td>51.3 ± 7.4</td>
<td>.010a</td>
</tr>
<tr>
<td>Physical component summary (mean ± SD)</td>
<td>43.9 ± 9.6</td>
<td>48.6 ± 7.3</td>
<td>.099</td>
</tr>
</tbody>
</table>

IQR, interquartile range.  
*aSignificant group difference, p<0.05.

for cancer survivors also had better physical functioning (6-m walk and 400-m walk) and body composition (waist + hip circumference, whole body fat mass). Notably, despite the potential clinically relevant 6-point difference between groups for bodily pain, these were not statistically significant. As a result, whether patients meeting the aerobic guidelines had less pain due to exercising or were able to meet the guidelines due to less pain has to be further explored in prospective studies. Furthermore, although not statistically significant, baseline clinical characteristics such as number of regions affected by bone metastases, time since cancer diagnosis and previous chemotherapy as well as comorbidities would suggest that those not meeting aerobic guidelines had more aggressive disease or that more symptoms may have impacted on their physical activity levels.

Treatment- and disease-related side effects as well as fear of skeletal fracture are likely to reduce physical activity levels in patients with bone metastatic prostate cancer. For the same reasons, clinicians are reluctant to refer these patients to exercise programmes (Galvao et al., 2011). However, inactivity is likely to increase fatigue, further decrease physical function and quality of life as well as increase the risk of other chronic diseases (Carlin & Andriole, 2000; Saad et al., 2004). Initial data from a pilot study involving a small sample suggest that resistance training may be well tolerated and effective (Cormie et al., 2013). Ongoing larger RCTs are examining the efficacy and safety of a modular multi-modal exercise programme, involving resistance, aerobic and flexibility exercise, in the same patient population (Galvao et al., 2011). In patients with non-metastatic prostate cancer the positive effects of exercise on muscle mass, physical function and quality of life are well supported. Apart from numerous randomised controlled intervention trials, recent and large cross-sectional studies show a relationship between physical activity levels and psychological distress, quality of life, and both all cause and prostate cancer mortality (Bonn et al., 2015; Galvao et al., 2015; Kenfield et al., 2011; Santa Mina et al., 2014). Our initial data would suggest that prostate cancer patients with bone metastases may similarly benefit from physical activity.

We recently reported from a large population based cohort study that ~21% of prostate cancer patients with localised disease met the current aerobic exercise guidelines (Galvao et al., 2015), as compared to ~29% of the prostate cancer patients with bone metastases in the present study. This is contrary to our original hypothesis that prostate cancer patients with bone metastases would have low levels of aerobic exercise. A potential reason for these differences is that in the current study patients were recruited for an exercise trial and as a result may already have an interest in exercise and undertake higher levels of activity compared to those not interested in exercise. Furthermore, considering the small sample size of the present study such a comparison should be undertaken with great caution, as the differences may be coincidental. Similar results were also found for levels of inactivity with ~48% of prostate cancer patients with localised disease and 42% of patients with bone metastatic prostate cancer not performing any moderate or vigorous physical activity. Lack of physical activity was also associated with poorer quality of life in the population of prostate cancer patients with localised disease (Galvao et al., 2015).

Our study has several features that are worthy of comment. We used a unique population of patients with advanced bone metastatic disease rarely reported in the literature in relation to physical activity and aerobic exercise participation. We included a comprehensive battery of measures of physical functioning and body composition. Despite our preliminary findings, our study has several limitations. The cross-sectional nature of the study does not permit us to infer cause and effect. Since we used baseline data of an exercise intervention trial, patients were only included if they did not have an acute illness, significant bone pain, musculoskeletal or cardiovascular or neurological disorders that could inhibit or put them at risk from exercising. Also, patients were excluded if they reported undertaking structured and supervised aerobic and/or resistance training two or more times per week within the past 3 months. Therefore, potentially patients with more severe disease/adverse events and very active patients were not considered in this analysis. For example, the SF-36 outcome “bodily pain” suggests that patients’ pain levels were similar to those of the general population. Thus, the data may not be representative of all bone metastatic prostate cancer patients. However, only one patient was excluded at study entry based on the criterion already participating.
in a structured exercise programme twice a week. Moreover, physical activity participation was by self-report and as such is subject to under- and over-reporting. We intentionally did not include resistance exercise in our analysis given that this exercise modality is not commonly prescribed in patients with advanced bone metastatic disease and only eight patients reported undertaking some form of resistance exercise at study entry. A further limitation is the relatively small sample size. In addition, given the number of comparisons made, it is possible that a few chance findings may have occurred. Future research is required to confirm and expand these findings in a larger sample size.

In summary, higher levels of aerobic exercise are associated with better physical and mental health outcomes in a unique population of prostate cancer survivors with bone metastases. Approximately, 29% of this patient population included in this analysis met aerobic exercise guidelines for cancer survivors. Further efforts are required to increase physical activity levels in prostate cancer patients with bone metastases as well as improve knowledge on the specific and unique requirements of exercise prescription for this population.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

All authors had no conflict of interest, including relevant financial interests, activities, relationships and affiliations to declare relating to this manuscript.

REFERENCES


TABLE 4 Objective measures of physical function and group differences with respect to meeting and not meeting the aerobic exercise guidelines

<table>
<thead>
<tr>
<th>Measure</th>
<th>Not meeting aerobic exercise guidelines (n = 39)</th>
<th>Meeting aerobic exercise guidelines (n = 16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual pace 6-m walk (s, median [IQR])</td>
<td>4.7 (4.4–5.3)</td>
<td>4.6 (4.3–4.8)</td>
<td>.046*</td>
</tr>
<tr>
<td>Fast pace 6-m walk (s, median [IQR])</td>
<td>3.4 (3.2–3.8)</td>
<td>3.0 (2.8–3.3)</td>
<td>.008*</td>
</tr>
<tr>
<td>400-m walk (s, mean ± SD)</td>
<td>258.1 ± 38.4</td>
<td>231.6 ± 24.0</td>
<td>.043*</td>
</tr>
<tr>
<td>Timed up and go (s, median [IQR])</td>
<td>7.4 (6.2–8.7)</td>
<td>6.3 (5.9–7.2)</td>
<td>.062</td>
</tr>
<tr>
<td>Waist circumference (cm, mean ± SD)</td>
<td>103.4 ± 10.9</td>
<td>95.9 ± 11.2</td>
<td>.038*</td>
</tr>
<tr>
<td>Hip circumference (cm, mean ± SD)</td>
<td>105.4 ± 7.2</td>
<td>101.9 ± 5.4</td>
<td>.035*</td>
</tr>
<tr>
<td>Whole body lean mass (kg, median [IQR])</td>
<td>55.2 (49.9–61.3)</td>
<td>55.6 (50.9–59.5)</td>
<td>.885</td>
</tr>
<tr>
<td>Whole body fat mass (kg, mean ± SD)</td>
<td>30.1 ± 7.2</td>
<td>25.0 ± 6.6</td>
<td>.014*</td>
</tr>
<tr>
<td>Whole body fat mass (%)</td>
<td>33.4 ± 3.8</td>
<td>29.4 ± 4.1</td>
<td>.002*</td>
</tr>
</tbody>
</table>

IQR, interquartile range. Usual pace 6-m walk (n = 55); fast pace 6-m walk (n = 53); 400-m walk (n = 33); timed up and go (n = 53).

*Significant group difference, p<0.05.


