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Original article

The characteristics of physical activity and gait in patients receiving radiotherapy in cancer induced bone pain

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ABSTRACT

Background and purpose: An objective measure of pain relief may add important information to patients' self assessment, particularly after a treatment. The study aims were to determine whether measures of physical activity and/or gait can be used in characterizing cancer-induced bone pain (CIBP) and whether these biomarkers are sensitive to treatment response, in patients receiving radiotherapy (XRT) for CIBP.
Materials and methods: Patients were assessed before (baseline) and 6–8 weeks after XRT (follow up). The following assessments were done: Brief Pain Inventory (BPI), *activ*PAL™ activity meter, and GAITRite® electronic walkway (measure of gait). Wilcoxon, Mann–Whitney and Pearson statistical analyses were done.
Results: Sixty patients were assessed at baseline; median worst pain was 7 and walking interference was 5. At follow up 42 patients were assessed. BPI worst pain, average pain, walking interference and total functional interference all improved ($p < 0.001$). An improvement in functional interference correlated with aspects of physical activity (daily hours standing $r = 0.469$, $p = 0.002$) and gait (cadence $r = 0.341$, $p = 0.03$). The *activ*PAL and GAITRite parameters did not change following XRT ($p > 0.05$). In responder analyses there were no differences in *activ*PAL and GAITRite parameters ($p > 0.05$).
Conclusion: Assessment of physical activity and gait allow a characterization of the functional aspects of CIBP, but not in the evaluation of XRT.

Cancer pain can be influenced by many factors such as psychological and emotional state, social circumstances and changes in functional ability, as well as the underlying disease [1]. This can make an accurate assessment of pain challenging. Cancer induced bone pain (CIBP) is one of the most common types of cancer pain, present in 28–45% of patients with bone metastases [2]. Radiotherapy (XRT) is the gold standard treatment for CIBP [3]. However, XRT is not effective in all patients. Complete pain relief is achieved in only about 25% of patients, while partial pain relief is achieved in 41–61% of the patients [4–6]. While the characteristics of those who respond to XRT for CIBP is not clear, one study has suggested that thermal characteristics of pain may predict response [7].

Patients' self assessment on a 0–10 numerical rating scale (NRS) is considered the standard method for assessing pain and quantifying analgesic response [8], but this is subjective and can be influenced by other factors than the pain stimuli. In CIBP, assessing response to interventions as XRT can be challenging, especially if multiple sites and types of pain exist. While patient rated assessments remain essential, surrogate markers of different aspects of pain may be useful in assessing the response to treatment. The IMMPACT Guidelines recommend that different dimensions of pain should be measured to assess treatment responses, including function [9]. The importance of assessing physical activity in CIBP has also been supported by others [10]. In patients with CIBP receiving XRT, evaluating the response to XRT using a biomarker of physical activity, may improve assessment of response by giving a wider evaluation of activity in addition to patient reported pain. Further characterization of the response to XRT using biomarkers may also

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make it possible to identify patients who are most likely to benefit. This would have advantages for health care resources, clinicians and patients.

As CIBP often affects the weight-bearing skeleton physical activity such as walking, may be reduced: therefore an indicator of better pain control may be improved physical activity. Although patient-rated assessment of pain, and its impact on function, is used routinely in the clinical setting, to date, few objective measures of physical functioning have been assessed. One of the marked features of CIBP is movement-related pain and it follows that successful treatment should effectively alleviate this. Accurate and objective measures of the impact of this movement-related pain are important to properly assess the efficacy of existing and novel analgesic interventions for CIBP.

Physical activity is usually assessed using performance status, which like assessment of gait, is subjective. One objective measure of physical activity is the *activ*PAL™ physical activity meter. This is a valid and reliable measure of walking [11], posture and motion [12]. It has been used in patients with chronic low back pain [13], in cancer patients with fatigue and weight loss [14], and in lung cancer patients treated with neuromuscular electrical stimulation [15]. Another study looked into how different stages of the disease and different treatment modalities affect physical activity in cancer patients [16]. However, the role of the *activ*PAL™ in the assessment of CIBP and response to XRT, has not been assessed.

Several different methods exist to assess gait. One method is the GAITRite® electronic walkway system. This objectively measures the spatial and temporal characteristics of gait, is a valid and reliable assessment tool [17–20], and has been used in patients with different conditions, including neurological conditions [21–24]. There are no reports of the use of the GAITRite® in the assessment of cancer pain. However, another computerized mat (GaitMat system, E.Q., Inc. Chalfont, PA) demonstrated a correlation between changes in gait parameters and pain severity in patients with anterior knee pain [25].

The primary aim of this study was to determine whether objective measures of physical activity and/or gait can be used as part of a comprehensive characterization of CIBP. A secondary aim was to examine whether these measures can be used as clinical biomarkers that are sensitive to treatment response, in patients receiving XRT for CIBP.

Materials and methods

The study was conducted at the Edinburgh Cancer Centre and had been granted ethical approval by the Local Research Ethics Committee.

The results presented are a secondary analysis of prospectively collected data from a translational study of the effects of XRT on somatosensory processing in CIBP [7]. A consecutive sample of patients who were due to receive XRT for CIBP, were recruited, over 18 months. Patients who were due to receive XRT for CIBP were assessed for eligibility. Eligible patients met the following criteria: diagnosis of CIBP secondary to bone metastases (histological or radiological evidence); $\geqslant$18 years; ECOG score $\leqslant$2 [26]. Patients were excluded if they had: pathological fracture at index pain site; spinal cord compression; confusion or significant psychiatric illness; unstable or rapidly deteriorating clinical condition. Following written informed consent, patients were assessed within 24 h of XRT (baseline) and 6–8 weeks after treatment for CIBP (follow up).

Patients completed the following at study baseline and follow up:

The Brief Pain Inventory (BPI) was used to assess pain [27,28]. It provides information on pain intensity as well as the degree to which pain interferes with function. The following scores were used: the single "worst pain" item; the single "average pain" item; the single "walking interference" item (possible score 0–10 for all three items (0 = no pain, 10 = worst pain)); and the total functional interference score (sum of all interference items, possible score 0–70). All pain assessments were specific to the site of CIBP treated (or to the worst site of CIBP if multiple areas). Responses after treatment referred only to the pain site assessed at baseline.

Activity – assessed using the *activ*PAL™ ambulatory physical activity meter (PAL Technologies Ltd., Glasgow, UK). This is a reusable, single unit device ($5.3 \times 3.5 \times 0.7$ cm, weight 20 gram), secured easily to the anterior thigh. The *activ*PAL™ uses an accelerometer to sense movement coupled with offline algorithms to generate the activity record. It records step number, and classifies an individual's free-living activity into periods spent sitting or lying, standing, and walking daily. The following were used as control values: steps per day: 9184 [29]; time sitting or lying: 16.8 hrs/day; standing: 5.0 hrs/day; and walking: 2.2 hrs/day [30]. The patients were asked to wear the monitor for 14 days.

Gait – assessed using a 4.3 meter GAITRite® electronic walkway (SMS Technologies Ltd., Harlow Essex, UK). This is a computer-based, instrumented walkway that measures spatial and temporal gait characteristics using embedded pressure sensors. Patients were instructed to walk along the GAITRite® walkway at a "normal" pace, two to four times, giving an average set of gait parameters. Velocity (cm/s), cadence (steps/minute) and Functional Ambulatory Performance score (FAP), a single score that represents the quantification of gait based on spatiotemporal parameters were examined. The following were used as control values: Normal mean velocity: 116 [17]; cadence: 108 [17]; and FAP: 95–100 [31].

At follow up patients were grouped as "responders" and "non-responders", in accordance with the guidelines "International consensus on palliative radiotherapy endpoints for future clinical trials in bone metastases" initially published in 2002 [32], and updated in 2011 [33]. Patients were classified as responders if they had complete or partial pain relief. Complete relief is defined as a pain reduction of two or more points in the BPI worst pain score, with no increase in analgesic intake. Partial pain relief is defined as either (i) pain reduction of two or more points in the BPI worst pain score together with no increase in analgesic intake, or (ii) reduction in analgesic intake of at least 25% from baseline without an increase in pain score. Patients were otherwise classified as non-responders ("pain progression" or "indeterminate response").

Statistical analysis

Demographics were summarized using proportions. Study assessments (pain, physical activity, and gait) were compared between baseline and follow up (Wilcoxon signed rank test). Responders and non-responders were compared (Mann–Whitney *U* test). Where follow up assessment was not conducted, patients were compared to those who completed, using the Mann–Whitney *U* test. Relationships between *activ*PAL™ parameters, GAITRite® parameters and BPI were examined using Pearson correlation coefficient (between 0.10 and 0.29 (weak relationship); 0.30 and 0.49 (moderate); 0.5 and 1.0 (strong)) [34]. A p value <0.05 was statistically significant. No correction was made for multiple testing because this was exploratory analyses. The data were not normally distributed, and unless stated, data are presented in medians and interquartile ranges (IQR). Statistical analysis was performed using SPSS 19.0 for Windows (SPSS INC., Chicago Illinois, USA).

Results

Sixty-one patients were consented, however one patient was withdrawn before baseline assessments; therefore sixty patients

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