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Comparison of posture and balance in cancer survivors and age-matched controls

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ABSTRACT

Background: The combination of peripheral neuropathy and other treatment-associated side effects is likely related to an increased incidence of falls in cancer survivors. The purpose of this study was to quantify differences in postural stability between healthy age-matched controls and cancer survivors.
Methods: Quiet standing under four conditions (eyes open/closed, rigid/compliant surface) was assessed in 34 cancer survivors (2 males, 32 females; age: 54(13) yrs., height: 1.62(0.07) m; mass: 78.5(19.5) kg) and 34 age-matched controls (5 males, 29 females; age: 54(15) yrs.; height: 1.62(0.08) m; mass: 72.8(21.1) kg). Center of pressure data were collected for 30 s and the trajectories were analyzed (100 Hz). Three-factor (group*-surface*vision) mixed model MANOVAs with repeated measures were used to determine the effect of vision and surface on postural steadiness between groups.
Findings: Cancer survivors exhibited larger mediolateral root-mean square distance and velocity of the center of pressure, as well as increased 95% confidence ellipse area ($P < 0.01$) when compared with their age-matched counterparts. For example, when removing visual input, cancer survivors had an average increase in 95% confidence ellipse area of 91.8 mm^2 while standing on a rigid surface compared to a 68.6 mm^2 increase for the control group. No frequency-based center of pressure measures differed between groups.
Interpretation: Cancer survivors exhibit decreased postural steadiness when compared with age-matched controls. For cancer survivors undergoing rehabilitation focused on existing balance deficits, a small subset of the center of pressure measures presented here can be used to track progress throughout the intervention and potentially mitigate fall risk.

1. Introduction

Understanding postural steadiness as purposeful movements to maintain equilibrium is essential to understanding human movement (Riley et al., 1990), particularly for clinical populations who exhibit postural deficits due to disease and treatments. Researchers have attempted to elucidate the underlying mechanisms of age related postural unsteadiness by comparing elderly individuals and healthy young adults (Hageman et al., 1995; Laughton et al., 2003; Manchester et al., 1989; Prieto et al., 1996). Prieto et al. (1996) showed that removal of visual input during quiet standing resulted in greater instability in elderly individuals, suggesting elderly adults (66–70 years) were less able to control their balance compared with young adults (21–35 years). Thus, when elderly adults relied on proprioceptive and vestibular input they were less able to control their balance (Prieto et al., 1996).

Postural stability in patients with diabetic neuropathy has also received considerable attention in the literature. Patients with moderate to severe peripheral diabetic neuropathy demonstrate less stability than patients without diabetic neuropathy or control groups suggesting that neuropathy, rather than the disease, is linked to instability (Oppenheim et al., 1999; Simoneau et al., 1994). Given that postural control requires visual, somatosensory and vestibular (Lord et al., 1993; Oppenheim et al., 1999; Prieto et al., 1996; Slobounov et al., 1997) inputs, it is unsurprising that neuropathy is detrimental to postural steadiness. Neuropathy is often found in patients with cancer as well, as a side effect of cancer treatments.

In the United States, nearly 1.69 million people were expected to be diagnosed with cancer in 2017 (American Cancer Society, 2017; Siegel et al., 2017). With overall survival rates approaching 70%, there are approximately 15.5 million cancer survivors in the United States

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(American Cancer Society, 2017; Siegel et al., 2017). Cancer treatments have been associated with detrimental side effects including pain, fatigue, depression, weakness, peripheral neuropathy, mobility limitations, balance impairments, and falls (Delanian et al., 2012; Silver and Gilchrist, 2011; Winters-Stone et al., 2011). Many neurotoxic chemotherapy drugs produce side-effects such as peripheral neuropathy (Wilkes, 2007), and vestibular dysfunction which may lead to decreased postural stability (Silver and Gilchrist, 2011). In particular, chemotherapy agents often result in axonal degeneration which may cause issues with both the sensory and motor neurons required to continuously maintain postural stability (Visovsky, 2003).

Several investigations have identified significantly higher fall rates among community-dwelling cancer survivors (Chen and Janke, 2014; Spoelstra et al., 2013; Wildes et al., 2015; Winters-Stone et al., 2011) compared to the average fall rate for older adults. While the annual fall rate for adults 65 years and older is ~30%, several studies have documented 56–58% of cancer survivors have fallen at least once within the past 12 months (Hornbrook et al., 1994; Huang et al., 2015; Spoelstra et al., 2013; Winters-Stone et al., 2011). The combination of peripheral neuropathy and other treatment-associated side effects is likely related to the increased fall risk often reported for cancer survivors. Current research in this area (Cianfrocca et al., 2006; Silver and Gilchrist, 2011; Tofthagen, 2010; Wilkes, 2007; Winters-Stone et al., 2011) tends to be limited to descriptions of balance deficits and dysfunction in cancer survivors without quantitative assessments to support these descriptions. One investigation by Wampler et al. (2007) assessed balance in breast cancer survivors using center of pressure (CoP) velocities and a pair of clinical tests (i.e., Timed Up and Go and the Fullerton Advanced Balance Scale). Their findings indicated decreased postural control in cancer survivors compared with healthy controls for both CoP velocity and the clinical measures. Although Wampler et al. found differences in both clinical and quantitative techniques, simple clinical tests, such as single limb stance or assessments that use pass/fail criteria, may not be sensitive enough to accurately detect differences in postural steadiness between healthy controls and cancer survivors (Balasubramanian, 2015; Battaglini et al., 2011; Pardasaney et al., 2012).

While there are a variety of tests to measure balance, from simple clinical tests to complex techniques (Faraldo-Garcia et al., 2012; Wampler et al., 2007), simple clinical tests have obvious limitations in measurement sensitivity, thus more sophisticated analysis techniques should be relied upon to characterize postural control when available. While it is redundant to use multiple highly-related measures to typify postural steadiness, it may also be necessary to use a small number of measures in order to adequately describe balance performance (Prieto et al., 1996). Quantitative assessments of postural steadiness in cancer survivors need to be performed to better understand the underlying causes of postural unsteadiness in this population.

The purpose of this study was to quantify differences in postural stability between healthy age-matched controls and cancer survivors during quiet standing. Moreover, this study attempts to quantify these differences under modified visual and surface conditions using measures of CoP trajectory. Our focus was on CoP based measures that were previously shown to be sensitive to changes in vision conditions and indicators of balance deficits, including fall risk, in older adults without cancer (Kurz et al., 2013; Prieto et al., 1996). Finally, this study sought to identify a subset of the investigated CoP based measures that best characterize postural stability in cancer survivors.

2. Methods

2.1. Participants

A convenience sample of cancer survivors entering a cancer rehabilitation program designed to help mitigate the detrimental side effects of their cancer treatments was recruited for this study. Participants included 34 cancer survivors (2 males, 32 females; age: mean 54 (SD 13) yrs., height: mean 1.62 (SD 0.07) m; mass: mean 77.5 (SD 19.5) kg; body mass index: mean 29.9 (SD 7.3) kg/m^2) in various stages of treatment and recovery. The participants in the study were selected consecutively over the course of 1 year from a larger patient population, provided they were able to safely stand unassisted for longer than 1 min. The group included breast (n = 20), colon (n = 4), skin (n = 1), brain (n = 1), ovarian (n = 1), prostate (n = 1), non-Hodgkin's lymphoma (n = 2), multiple myeloma (n = 1), leukemia (n = 1), lung (n = 1), and kidney/liver (n = 1) cancers. Overall, 94% of the subjects underwent surgery, 32% had radiation treatment, and 71% had chemotherapy treatment. At the time of assessment, 21% of patients were still undergoing radiation or chemotherapy treatment. A table provided as supplemental material provides more subject specific information on the group of cancer survivors (Supplementary Table 1). Thirty-four healthy adults (5 males, 29 females; age: mean 54 (SD 15) yrs.; height: mean 1.62 (SD 0.08) m; mass: mean 72.8 (SD 21.1) kg; body mass index: mean 27.7 (SD 6.6) kg/m^2) free from neurologic and vestibular impairments were recruited to serve as an age-matched control group. Body mass index (BMI) was similar between groups. No significant differences were found between groups for any group characteristic described above. Each participant provided informed written consent prior to participation in the balance assessment. The University's Institutional Review Board approved the protocol.

2.2. Data acquisition

Participants completed four quiet standing tests without shoes in the following order: 1) rigid surface with eyes open (RSEO), 2) rigid surface with eyes closed (RSEC), 3) compliant surface with eyes open (CSEO), and 4) compliant surface with eyes closed (CSEC). A single trial for each condition was completed in the standardized order. No familiarization trials were performed. Prior to assessments, feet were placed at a self-selected width, symmetrical about the mid-line with medial malleoli aligned with markings on the plate running from medial-to-lateral. The positions of the feet were measured to maintain position when switching to the compliant surface. The compliant surface consisted of a 3 in medium density foam block used to alter the proprioceptive feedback from the feet. The compliant surface also served to disrupt postural control by decreasing the effectiveness of adjustments made at the foot and ankle to maintain static balance (Patel et al., 2008). During assessments, participants focused on a visual target located at eye-level 1 m away. For conditions with the eyes closed, participants began by staring at the visual target and closed their eyes on a verbal cue. A harness was used during all testing conditions for safety. Force and CoP data (1000 Hz) were collected using Bertec's BalanceCheck™ system (Bertec Corp, Columbus, OH, USA) for 30 s for each condition.

2.3. Data analysis

Data were exported and further processed using custom software (MATLAB r2010a, MathWorks, Lowell, MA, USA). Based on previous literature (Prieto et al., 1996), data were resampled at 100 Hz for analysis. CoP data were filtered using a digital Butterworth fourth-order, zero lag, low pass filter with a cutoff frequency of 5 Hz. Only the middle 28 s of data from each trial were used in calculations to avoid any perturbations caused by initiation and conclusion of the data collection trial. The following time domain measures of CoP motion were computed using algorithms previously defined in the literature (Prieto et al., 1996): root-mean square distance (RMS) of the anterior-posterior (AP), and medial-lateral (ML) CoP; mean velocities of AP and ML CoP; and 95% confidence ellipse (CE) area. In addition, the frequency domain measures computed were: mean AP and ML CoP frequencies, and 95% power frequency of the AP and ML CoP.