JOURNAL OF GERIATRIC ONCOLOGY 7 (2016) 108–115

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Patient-reported versus objectively-measured physical function and mortality risk among cancer survivors

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ARTICLE INFO

Article history:
Received 12 August 2015
Received in revised form 28 December 2015
Accepted 29 January 2016
Available online 18 February 2016

Keywords:
Physical function
Aging
Oncology
Disability
Physical activity
Exercise

ABSTRACT

Objective: This study aimed to characterize the relationship of patient-reported functional limitations, gait speed, and mortality risk among cancer survivors.
Materials and Methods: This study included cancer survivors from the Third National Health and Nutrition Survey. Patient-reported functional limitations were quantified by asking participants to assess their ability to complete five tasks: (1) walking 1/4 mi, (2) walking up 10 steps, (3) stooping, crouching, or kneeling, (4) lifting or carrying an object of 10 lb, and (5) standing up from an armless chair. Gait speed was quantified using a 2.4-meter walk. Vital status was obtained through the United States National Center for Health Statistics.
Results: The study sample included 428 cancer survivors who averaged 72.1 years of age. The average number of patient-reported functional limitations was 1.8 (out of 5) and 66% of participants reported ≥1 functional limitation. Patient-reported functional limitations and gait speed were related, such that each functional limitation associated with a −0.08 m/s slower gait speed (95% confidence interval: −0.10 to −0.06; $P < 0.001$). During a median follow-up of 11 years, 329 (77%) participants died. In multivariable-adjusted analysis, patient-reported functional limitations and survival were related, such that each additional reported functional limitation was associated with a 19% increase in the risk of death (95% confidence interval: 9% to 29%; $P < 0.001$).
Conclusion: Patient-reported functional limitations are prevalent among cancer survivors, and associate with slower gait speeds and shorter survival. These data may provide increased insight on long-term prognosis and inform clinical decision-making by identifying subgroups of cancer survivors who may benefit from rehabilitative intervention.

1. Introduction

The assessment of functional limitations is an important component for evaluating the overall health and physiologic reserve of cancer survivors.[1–3] After a diagnosis of cancer, patient-reported physical function deteriorates at an accelerated rate compared to that of age-matched cancer-free persons.[4,5] This may be a result of cancer treatment, which impairs multiple physiologic systems such as cardiopulmonary,[6,7] neurologic,[8] and musculoskeletal systems,[9,10] which are necessary to enable physical function. Treatment-related physiologic impairments may explain why cancer survivors are up to nine-fold more likely to report a functional limitation compared to similar-aged persons without a history of cancer.[11,12]

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http://dx.doi.org/10.1016/j.jgo.2016.01.009
1879-4068/

Clinicians that appropriately characterize functional limitations may have unique insight into their patients' risk of progression in the disablement pathway.[13] Options to measure functional limitations include validated objective metrics of physical function such as gait speed, also known as walking speed, which predicts survival among older adults and cancer survivors.[14,15] Gait speed is also associated with cognitive impairment, cardiopulmonary disease, hospitalization, and nursing home placement.[16] Alternatively, implementing patient-reported outcomes of physical function may be more feasible in clinical practice, but studies to date have not confirmed that patient-reported functional limitations correlate with objectively measured physical function, such as gait speed, among cancer survivors.

Identifying clinical assessments that accurately risk-stratify patients who have survived cancer will benefit care providers and scientists in targeting therapies to the most vulnerable cancer survivors. Therefore, the goal of this study was to characterize the association between patient-reported functional limitations and objectively measured physical function (i.e., gait speed), and describe the relationship between patient-reported functional limitations and mortality risk among a population-based sample of cancer survivors.

2. Methods

2.1. Study Design

The Third National Health and Nutrition Examination Survey, 1988–1994 (NHANES III) was a stratified multistage study designed to provide health information on a nationally representative sample of US civilians.[17] A stratified multistage sampling design was used to select participants that were representative of the US population. The four sampling stages included: 1) counties within states; 2) city blocks within each county; 3) households within each city block and; 4) individuals within each household. The study protocol for NHANES III was approved by the National Center for Health Statistics of the Centers for Disease Control and Prevention Institutional Review Board. All participants provided written informed consent prior to participating in any study-related activities.

2.2. Study Participants

Participants aged ≥60 years were invited to complete an evaluation that included patient-reported measures of functional limitations and objective measures of physical function.[18] We identified 4881 participants who completed the requisite study measures, 428 (9%) of whom reported a prior diagnosis of non-skin-related cancer.

2.3. Patient-Reported Functional Limitations

Functional limitations were assessed by asking the participants to report the level of difficulty for five common tasks that included: (1) walking for a quarter of a mile, (2) walking up 10 steps, (3) stooping, crouching, or kneeling, (4) carrying something as heavy as 10 pounds, and (5) standing up from an armless chair. For each question, the participants were provided answers of: (1) no difficulty, (2) some difficulty, (3) much difficulty, and (4) unable to do. The participants who reported at least some difficulty were considered to have functional limitation in that task.[19–21] The participants who reported limitations in three or more tasks were classified as disabled.[19]

2.4. Objectively-Measured Physical Function

Gait speed is an objective measure that quantifies overall health and functional ability,[15,22] and has been shown to predict survival among cancer survivors.[14] Gait speed was assessed using a 2.4-meter walk on a straight and level surface.[18] The time required to complete the 2.4-meter course was recorded to the nearest tenth of a second using a stopwatch. Gait speed was quantified in units of meters per second (m/s), by dividing 2.4 m into the number of seconds required to complete the walk.

2.5. Mortality Outcome

The primary outcome of this study was death from any cause. Vital status was identified using the National Death Index (NDI) database on December 31, 2006. The participants were linked to the NDI database using a probabilistic matching algorithm that included 12 identifiers including Social Security number, sex, date of birth, race, state of residence, and marital status.[23] The United States National Center for Health Statistics found that 96.1% of deceased participants and 99.4% of living participants were correctly classified using the probabilistic matching algorithm.[24]

2.6. Covariates

Demographic information including date of birth and sex were patient-reported using a standardized questionnaire. Clinical information including type of cancer, date of cancer diagnosis, smoking history, alcohol consumption, hospitalizations in the prior year, patient-reported health status, and frequency of physical activity were assessed using standardized questionnaires. Bouts of walking in the past week were patient-reported and included any bout of walking that was estimated to be ≥1 mi in duration, and of moderate or vigorous intensity. The presence of comorbid health conditions was determined by asking the participants if a doctor had ever told them that they had any of the following: hypertension, diabetes, hyperlipidemia, asthma, arthritis, myocardial infarction, stroke, or congestive heart failure.

Height in meters and weight in kilograms were measured by study technicians. Body mass index was calculated as weight divided by the square of height (kg/m^2). The healthy eating index (HEI) was calculated from 24-hour food recalls to form a score that ranges from 0 to 100 to quantify aspects of a healthy diet.[25] Hemoglobin was quantified using a Coulter S-Plus Jr. electronic counter (Coulter Electronics, Hialeah, FL, USA) with a coefficient of variation of <3.0%. Albumin was quantified using a Hitachi 737 multichannel analyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN, USA) with a coefficient of variation of <2.8%. C-reactive protein was quantified using latex-enhanced nephelometry immunoassay (Behring Diagnostics, Somerville, NJ, USA) with a coefficient of variation of <6.3%. Detailed blood collection procedures and