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Self-reported major mobility disability and mortality among cancer survivors

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ABSTRACT

Objective: To quantify the prevalence of self-reported major mobility disability (SR-MMD) and its association with mortality in a nationally-representative sample of cancer survivors.
Materials and Methods: This study included patients with a history of cancer who participated in the National Health and Nutrition Examination Survey 1999—2010. SR-MMD was defined as self-reported difficulty or inability to walk a quarter of a mile. Vital status through December 15, 2011 was ascertained from the United States National Center for Health Statistics. Multivariable-adjusted Cox regression models were used to quantify the hazard ratio (HR) and 95% confidence interval (CI) between SR-MMD and mortality.
Results: The study included 1458 cancer survivors who averaged 67.1 years of age. At baseline, 201 (13.7%) participants had SR-MMD. During a median follow-up of 4.7 years, 434 (29.8%) participants died. SR-MMD was independently associated with a higher risk of all-cause mortality [HR: 2.15 (95% CI: 1.56–2.97); $P < 0.001$] and cancer-specific mortality [HR: 2.49 (95% CI: 1.53–4.07); $P < 0.001$]. The association between SR-MMD and all-cause mortality was not modified by age, sex, time since cancer diagnosis, body mass index, or comorbid health conditions.
Conclusion: SR-MMD is an easily ascertainable metric of physical function that is associated with a higher risk of mortality among cancer survivors. Integrating measures of physical function may help to guide clinical decision-making and improve long-term prognostication in this population. Interventions that prevent the development of SR-MDD, such as physical activity, should be evaluated in this population.

1. Introduction

Physical function is an important determinant of health-related quality-of-life among cancer survivors [1]. After a diagnosis of cancer, physical function deteriorates at an accelerated rate compared to that of age-matched cancer-free individuals [2]. It is hypothesized that cancer and its treatments impair the cardiovascular, pulmonary, neurologic, and musculoskeletal systems that are required to sustain adequate physical function [3,4]. Consequently, 57—66% of cancer survivors report at least one functional limitation, and many of these limitations persist for years after completing cancer treatment [5–7].

The ability to walk 400 m (approximately a quarter of a mile) is an objective measure of functional independence [8], and predicts the ability to safely ambulate in the community [9]. Major mobility disability (MMD) is defined as the inability to walk 400 m without the use of a walker (use of a cane is acceptable) [10]. MMD is prognostic of several important outcomes in older adults, including all-cause mortality and incident cardiovascular disease [11]. Despite the importance of objectively defined MMD, implementing the 400 m walk in practice may not be feasible given the need for a walking course of considerable length and dedicated staff time for in-person supervision [12]. To circumvent this issue, self-reported difficulty or inability to walk a quarter of a mile was validated as a proxy for objectively defined MDD [13,14].

Given the unique functional consequences of cancer and its treatments, and the validation of self-reported MDD (SR-MMD), this study aimed to achieve four objectives using a nationally-representative sample of cancer survivors. The first goal was to estimate the prevalence of SR-MMD among community-dwelling cancer survivors in the United States (US). Second, we sought to quantify the association between SR-MMD and all-cause and cancer-specific mortality. Third, we aimed to quantify the association between SR-MMD and all-cause mortality within specific subgroups. Our fourth and final goal was to assess whether there is evidence of a dose-response between self-reported degree of difficulty walking one quarter of a mile and all-cause and cancer-specific mortality.

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2. Materials and Methods

2.1. Study Design

The National Health and Nutrition Examination Surveys (NHANES) are a series of consecutive cross-sectional studies designed to provide health information on a nationally-representative sample of non-institutionalized United States civilians. Participants reside in counties across the country, fifteen of which are visited annually. The current analysis used six consecutive cycles of NHANES data from 1999 to 2010. The study protocol 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 engaging in any study related activities.

2.2. Study Participants

NHANES participants included were males and females, aged ≥21 years, with a self-reported history of cancer (excluding non-melanoma skin cancer). Participants were also required to have the requisite measure necessary to define SR-MMD (described below).

2.3. Self-reported Major Mobility Disability

SR-MMD was defined using a single question that asked participants to report "By yourself and without any special equipment, how much difficulty do you have walking for a quarter of a mile (that is about 2 or 3 blocks)"? Participants were not explicitly advised what modalities are included in the term "special equipment." Possible responses included: "no difficulty", "some difficulty", "much difficulty", or "unable to do". The two responses of "much difficulty" and "unable to do" were used to define the presence of SR-MMD [13].

2.4. Mortality Outcome

The primary outcome of this study was all-cause mortality, defined as the time from assessment of SR-MMD to death from any cause. The secondary study outcome was cancer-specific mortality, defined as the time from assessment of SR-MMD to death attributable to cancer. Vital status was identified using the National Death Index database on December 31, 2011. Participants were linked to the National Death Index database using a probabilistic matching algorithm that included 12 identifiers, such as Social Security Number, sex, date of birth, race, state of residence, and marital status [15].

2.5. Covariates

Demographic information including date of birth and sex, race, annual household income, and clinical information, including type of cancer, date of cancer diagnosis, and smoking history were ascertained from standardized participant questionnaires. Body mass index (BMI; kilograms (kg) per meter (m) squared; kg/m^2) was calculated using participant height (m) and weight (kg), as measured by a study technician, and then categorized as underweight, normal weight, overweight, and obese using the World Health Organization definitions [16]. Participation in any physical activity was defined as self-reported engagement in at least one bout of moderate- or vigorous-intensity physical activity of ≥10 min in duration within the past month. Self-rated health status was assessed using the first question of the SF-36 questionnaire [17]. The presence of comorbid health conditions was ascertained from participant responses to the question of whether a doctor had ever told them that they had any of the following: type 2 diabetes mellitus, myocardial infarction, stroke, and/or congestive heart failure.

2.6. Statistical Analysis

Descriptive variables are presented as means and standard errors for continuous variables and percentages for categorical variables. We fit multivariable logistic regression models to estimate the Odds Ratio (OR) and 95% Confidence Interval (CI) to determine demographics and clinical characteristics that were associated with cohort inclusion. We fit Cox proportional hazards regression models to estimate the Hazard Ratio (HR), and 95% CI for SR-MMD and the time-to-death outcomes. Models were first adjusted for sex and age (model 1) and then fully adjusted for demographic, behavioral, and clinical characteristics (model 2). The assumption of proportional hazards was confirmed using log-log plots. We incorporated a statistical interaction term into the regression models to determine if the observed associations were modified by certain a priori designated patient and clinical characteristics, with these results presented as subgroup analyses to facilitate interpretation. Sample weights were integrated into all statistical analyses to account for nonresponse bias, multistage sampling probabilities, and the subpopulation of participants that were included in this analysis. Sensitivity analyses were conducted to quantify the strength that an

Table 1
Demographic and clinical characteristics ($N = 1458$).

Characteristic	Mean ± standard error or *N* (%)
Age, years	67.1 ± 0.5
Sex	
Male	41.7%
Female	58.3%
Race and ethnicity	
Non-Hispanic White	84.5%
Non-Hispanic Black	7.4%
Other	8.1%
Annual household income	
<$25,000	31.2%
≥$25,000–$74,999	46.5%
≥$75,000	11.3%
Refused, unknown, missing	11.0%
Type of cancer	
Breast	23.7%
Gastrointestinal	10.9%
Genitourinary	22.7%
Gynecologic	15.7%
Lung/thoracic	5.6%
Hematologic	4.4%
Melanoma	7.8%
Other/don't know	9.3%
Time since cancer diagnosis, years	
Mean (continuous)	10.8 ± 0.4
<5	33.7%
5—10	25.3%
≥10	41.0%
Body mass index, kg/m^2	
Mean (continuous)	28.1 ± 0.2
<18.5	2.4%
18.5—24.9	28.3%
25.0—29.9	40.9%
≥30.0	28.4%
Smoking	
Never	41.6%
Former	43.5%
Current	14.8%
Physical activity, past month	34.7%
Self-rated health status	
Excellent	7.6%
Very good	27.4%
Good	41.5%
Fair	18.4%
Poor	5.1%
Conditions	
Type 2 diabetes	13.3%
Myocardial infarction	8.7%
Stroke	7.2%
Congestive heart failure	6.0%

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