Prevalence of Self-Reported Memory Problems in Adult Cancer Survivors: A National Cross-Sectional Study

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Abstract

Purpose: Cancer and its treatments can impair cognitive function, especially memory, leading to diminished quality of life. Prevalence studies of cancer treatment-related memory impairment have not been conducted in the adult-onset cancer population.

Methods: To determine the prevalence of self-reported memory (SRM) problems in people with and without a history of cancer, we analyzed data from a large, nationally representative sample of the civilian, noninstitutionalized US population. Participants answered the yes-or-no question, "Are you limited in any way because of difficulty remembering or because you experience periods of confusion?" Age, sex, race/ethnicity, education, poverty, and general health were controlled.

Results: The sample (N = 9,819) consisted of 4,862 men and 4,957 women age 40 years and older. There were 1,938 blacks,

5,552 whites, 1,998 Hispanics, and 331 participants categorized as other race/multiracial. Of these, 1,305 reported a history of cancer; 8,514 did not. Memory problems were self-reported more often by participants with a history of cancer (14%) than by those without (8%). Having had cancer was independently associated with SRM impairment (adjusted odds ratio, 1.4; 95% CI, 1.08 to 1.83). Other predictors of memory impairment were age, lower education, lower income, and poorer general health ($P < .01$ for all). Participants with cancer had a 40% greater likelihood of reporting memory problems relative to those without cancer.

Conclusion: Cancer history independently predicted SRM impairment. Prevalence of SRM impairment in people with a history of cancer/cancer treatment is substantial and increasing. Health care providers should assess and be ready to treat memory impairment in patients with a history of cancer.

Introduction

Cancer is a major public health problem in the United States, where approximately 10.8 million people have this diagnosis.¹ Worldwide, the annual incidence of cancer is estimated to be more than 10 million people, and it is projected to be approximately 15 million by 2020, making cancer a leading cause of death globally.² Currently, more than 28 million people worldwide have cancer, and this number could triple by 2030.³ In addition to these increases, improved treatments will likely increase the number of cancer survivors even more.

Cancer-related adverse effects include impaired attention, memory, processing speed, and executive function, in addition to the more generally known physical adverse effects such as fatigue, pain, nausea and emesis, and sleep dysfunction.⁴⁻⁹ Impairment in these cognitive functions sometimes interferes with the basic tasks of daily living, thereby diminishing quality of life.⁵⁻⁹ Preliminary studies have also shown that deficits in attention/mental flexibility or working memory predict nonadherence to medications among women with early-stage breast cancer receiving hormonal therapy.¹⁰ Unfortunately, fewer data are available on cancer-related cognitive dysfunction (CRCD) than on other cancer-related adverse effects. Current estimates of the prevalence of CRCD range from 17% to 75%,¹¹⁻¹⁶ and this prevalence is higher among patients with cancer than it is among healthy controls.¹¹⁻¹⁶ However, most of these estimates are from studies of women with breast cancer. These studies are generally small, single-center trials of homogeneous racial/eth-

nic and sociodemographic populations (predominantly educated, middle-class white women). In addition, the underlying neurobehavioral and biopsychologic mechanisms of CRCD resulting from cancer and its treatments on cognition are difficult to assess. In this study, we determined the prevalence of CRCD in a large, nationally representative sample of the US population. We looked for an independent association between a history of cancer and CRCD and controlled for several sociodemographic variables and potential confounders. We also determined whether this prevalence differed from that in people without a history of cancer.

Methods

Sample Description

We studied participants in the National Health and Nutrition Examination Survey (NHANES) from 2001 to 2006, a nationally representative, stratified, multistage probability sample of the civilian, noninstitutionalized population of the United States.^{17,18} Data collection methods included an interviewer-administered questionnaire using computer-assisted interviewing technology and physical examinations performed in mobile examination centers. Standardized collection methods were used to minimize site-specific errors. In addition, NHANES data collection involved oversampling of blacks, Hispanics, and persons age 60 years and older to facilitate computation of more reliable and representative statistics and to increase the preci-

sion of estimates.¹⁹ We restricted age ranges to correspond with those of other studies on cancer-related cognitive problems. Individuals with brain tumors were excluded because treatments (eg, surgery, radiation, and chemotherapy) for brain tumors are expected to be associated with cognitive problems resulting from direct damage to brain tissue.

Determination of Memory Problems

We assessed memory problems with self-reported responses (yes or no) to the following question from the Physical Functioning section of the NHANES Questionnaire: "Are you limited in any way because of difficulty remembering or because you experience periods of confusion?" Those who declined to answer or answered "Don't know" were counted as missing data.

Determination of Cancer Status

We assessed cancer status from the Medical Conditions section of the NHANES Questionnaire self-reported response to the question: "Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?" Those who declined to answer or gave an answer of "Don't know" were counted as missing data. The exclusion criterion of brain tumor was determined by the response to the follow-up question, "What kind of cancer?"

Description of Covariates

We assessed the following demographic covariates: age (ranges 40 to 44, 45 to 54, 55 to 64, and 65 or more years), race/ethnicity (Mexican American/other Hispanic; non-Hispanic white; non-Hispanic black; and other race, including multiracial), sex, education (less than high school; high school diploma, including general equivalency diploma; more than high school), and household income as a percent of the federal poverty level (< 100%, 100% to < 200%, 200% to < 300%, and 300% to < 500%). We also considered self-rating by participants of their general health condition as excellent, very good, good, fair, or poor.

Statistical Analyses

We estimated the prevalence of CRCD in the US population by weighting our results proportionally. Associations were determined on the basis of significant *P* values calculated with χ^2 tests for association. We used logistic regression to assess the independent association between cancer history and memory problems while controlling for age, race/ethnicity, sex, education, poverty/income ratio, and general health condition.

The NHANES sampling design is complex and involves stratification, clustering, and oversampling of subgroups to increase the reliability and accuracy of estimates. However, this clustering design and its incorporated differential probabilities of selection result in an unequal probability of selection. Consequentially, our statistical analyses incorporated stratum, primary sampling units, and appropriate sampling weights to produce unbiased estimates of the noninstitutionalized US population.

All statistical analyses were conducted using SAS-Callable SUDAAN Version 10.0.0 and SAS Version 9.2 (SAS Institute, Cary, NC). Alpha was set at 0.05, and all tests were two tailed.

Results

The sample consisted of 9,819 individuals (4,862 men; 4,957 women) age 40 years and older from diverse educational and racial/ethnic backgrounds: 1,938 blacks, 5,552 whites, 1,998 Hispanics, and 331 participants categorized as other race or multiracial. Of the total, 1,305 participants reported having had cancer, and 8,514 reported not having had cancer (Table 1).

Memory problems were self-reported by more participants who had had cancer (14%) than by those who had not (8%). Participants with cancer had a 40% greater likelihood of reporting memory problems relative to those without. In a logistic regression model, having had cancer was independently associated with self-reported memory impairment (adjusted odds ratio, 1.4; 95% CI, 1.08 to 1.83). Overall, cancer history, older age, greater poverty, non-Hispanic background, and poor general health were significantly and independently associated with a greater likelihood of reporting memory problems that affect daily functioning (Table 2). Participants reporting impaired memory were generally older non-Hispanic white women (Table 3).

Participants who had cancer and reported memory problems that interfered with activities of daily functioning varied in sociodemographic background (Table 1). However, our analysis did not reveal any predictive higher risk for memory problems based on the combined effects of these sociodemographic variables (*P* > .05).

We also examined possible interactions between cancer and sociodemographic variables to determine whether these characteristics put patients with cancer and cancer survivors at greater risk for cognitive problems. Only age increased risk (*P* < .001). However, the difference in reported memory problems was greater at younger ages (< 55 years) for patients with cancer (*P* < .001) than at older ages. That is, the odds ratio for cancer and memory problems decreased as age increased.

Discussion

The prevalence of CRCD in studies of mostly involving patients with breast cancer is between 17% and 75%. We found that CRCD was reported by 14% of participants who had cancer and by 8% of those who did not. The lower prevalence of self-reported memory problems in our study probably reflects the fact that our analysis included a greater variety of cancer types (every cancer except brain tumors) and was likely based on variable times since diagnosis and treatment. That a history of cancer was associated with a 40% higher rate of self-reported memory problems underscores the potential public health importance of this understudied problem.

We found a positive association between age and reported memory problems (Table 3), as expected, given the literature on this topic when we examined the entire sample. However, examination of the cancer subsample revealed a relationship between cancer history and memory for younger persons but not older persons. Specifically, memory problems were greater among participants younger than 55 years of age. This finding could be the result of many factors. First, the sample included substantially more individuals who had not had cancer. Thus, the expected relationship between older age and memory prob-

Table 1. Participant Characteristics

Characteristic	Cancer				P
	Yes (n = 1,305)		No (n = 8,505)		
	No.	%*	No.	%*	
Memory problems					< .001
Yes	183	13.5	706	8.3	
No	1,122	86.5	7,799	91.7	
Age, years					< .001
40 to 44	86	6.6	1,658	19.5	
45 to 54	287	22.0	3,062	36.0	
55 to 64	256	19.6	1,752	20.6	
≥ 65	676	51.8	2,033	23.9	
Race/ethnicity					< .001
Mexican American/other Hispanic	34	2.6	774	9.1	
Non-Hispanic white	1,173	89.9	6,404	75.3	
Non-Hispanic black	69	5.3	919	10.8	
Other race (including multiracial)	29	2.2	408	4.8	
Sex					< .001
Male	538	41.2	4,082	48.0	
Female	767	58.8	4,423	52.1	
Education					.9
< High school	240	18.4	1,616	19.0	
High school diploma (including GED)	343	26.3	2,220	26.1	
> High school	722	55.3	4,669	54.9	
Percentage of federal poverty level (based on household income relative to size)					< .1
< 100	87	6.7	808	9.5	
100 to < 200	282	21.6	1,590	18.7	
200 to < 300	208	15.9	1,327	15.6	
300 to < 500	359	27.5	2,296	27.0	
> 500	371	28.4	2,483	29.2	
General health condition					< .001
Excellent	128	9.8	1,046	12.3	
Very good	401	30.7	2,866	33.7	
Good	449	34.4	3,028	35.6	
Fair	240	18.4	1,293	15.2	
Poor	87	6.7	281	3.3	

Abbreviation: GED, general equivalency diploma.

* Column percentages reported are weighted to US population. Denominator is either those with memory problems (yes) or those without (no).

lems was confirmed. However, in the cancer sample, memory problems were inversely associated with age. The observed findings could also be the result of several differences between younger and older participants. For example, younger participants in the sample could be involved in work or other social environments and interactions in which cognitive dysfunction, especially declining memory, is much more noticeable than in older participants. The observed age difference could also be the result of a greater willingness of younger patients to report memory problems. Differences in treatment (chemotherapy dosage, radiation exposure) may also affect the rate of reported

Table 2. Effect of Cancer on Self-Reported Memory Impairment (N = 9,819)

Predictor	Adjusted Odds Ratio of Reporting Impaired Memory	95% CI
Cancer		
Yes	1.40	1.08 to 1.83
No	1.00	1.00 to 1.00
Age, years		
40 to 44	1.00	1.00 to 1.00
45 to 54	1.04	0.71 to 1.53
55 to 64	1.18	0.78 to 1.76
≥ 65	2.02	1.37 to 2.97
Race/ethnicity		
Mexican American/other Hispanic	0.79	0.60 to 1.04
Non-Hispanic white	1.00	1.00 to 1.00
Non-Hispanic black	1.12	0.91 to 1.38
Other race (including multiracial)	1.12	0.65 to 1.93
Sex		
Male	1.00	1.00 to 1.00
Female	1.09	0.94 to 1.29
Education		
< High school	1.39	1.11 to 1.74
High school diploma (including GED)	1.03	0.82 to 1.29
> High school	1.00	1.00 to 1.00
Percentage of federal poverty level (based on household income relative to size)		
< 100	4.07	2.67 to 6.20
100 to < 200	2.22	1.60 to 3.08
200 to < 300	2.12	1.47 to 3.05
300 to < 500	1.66	1.17 to 2.34
> 500	1.00	1.00 to 1.00
General health condition		
Excellent	1.00	1.00 to 1.00
Very good	1.81	1.10 to 2.98
Good	2.76	1.81 to 4.20
Fair	5.79	3.69 to 9.08
Poor	11.17	6.65 to 18.77

NOTE. Bold font indicates statistical significance at .05.

Abbreviation: GED, general equivalency diploma.

CRCD; however, with the present data, we could not examine this relationship. Additional studies could use well-calibrated cognitive performance tests to help determine whether younger patients with cancer simply notice the memory problem more because they have higher baseline memory abilities than do older patients with cancer, or because the older individuals have a higher expectation that they will have memory difficulties and so do not label memory deficits as problems to the same degree as younger individuals who do not have this same expectation.

Although not yet tested, it is possible that participants with CRCD might not be willing or able to participate in clinical cancer research. Neurocognitive dysfunction is a potentially

Table 3. Difference in Memory Problems

Age Range, Years	Exponentiated Contrast (HR for comparison)	95% CI
Cancer v no cancer		
40-44 v 40-44	4.43	2.11 to 9.31
45-54 v 45-54	2.19	1.14 to 4.23
55-64 v 55-64	1.16	0.57 to 2.37
≥ 65 v ≥ 65	1.07	0.76 to 1.50
Cancer v cancer		
45-54 v 40-44	0.55	0.20 to 1.46
55-64 v 40-44	0.36	0.12 to 1.07
55-64 v 45-54	0.65	0.26 to 1.62
≥ 65 v 40-44	0.59	0.28 to 1.22
≥ 65 v 55-64	1.64	0.82 to 3.30
No cancer v no cancer		
45-54 v 40-44	1.10	0.75 to 1.63
55-64 v 40-44	1.36	0.89 to 2.09
≥ 65 v 40-44	2.44	1.62 to 3.68

Abbreviation: HR, hazard ratio.

debilitating adverse effect of cancer and its treatments. Cognitive impairment has a negative effect on clinical decision making among patients with cancer,²⁰⁻²² and severe cognitive impairment has been reported in decisions to decline life-prolonging therapy and nonadherence to medication recommendations among women with early-stage breast cancer undergoing hormonal therapy.²³

In this cross-sectional study, we could not determine to what extent memory problems changed over time or which cancer stages and treatments might contribute to self-reported memory problems. We also could not exclude the potential of unmeasured confounding effects from other factors. We did not assess the degree of impairment, which would be necessary to ascertain the full implications of the problem. Although participants were screened with the question, "What kind of cancer?" to identify those with brain tumors, the data did not support reliable analysis by cancer type. We did not assess whether time from diagnosis, cancer type, or both affects memory because we did not have data on the specific time of diagnosis and because cancer type could not be verified. In addition, such analyses are likely to be biased by survival effects. Longer time since diagnosis could be confounded by cancer stage and type. For example, participants with late-stage disease or deadly cancers, such as lung and pancreatic cancers, may not have been well enough to be included in the sample. Additionally, the present study assessed memory problems by patient self-reported questionnaire instead of objective neuropsychologic measures. However, to date, there are no gold-standard measures of CRCD. Albeit subjective and possibly lacking psychometric rigor, patient self-reported complaints of CRCD could well precede clinical findings of neurocognitive impairments. Additional studies are needed that more systematically control for plausible alternative explanations of CRCD (eg, use of medication), evaluate broader

domains of cognitive function (eg, attention, memory, processing speed, and executive function) that could be affected by cancer and cancer treatments (eg, chemotherapy, radiotherapy), and more reliably estimate the prevalence of these debilitating adverse effects.

The prevalence of self-reported CRCD in a large, nationally representative sample of the US population was 14%. Participants with a history of cancer had a 40% greater likelihood of having memory problems than those without a history of cancer. Our findings showed a positive relationship between age and self-reported memory problems for the entire sample. However, a subsample examination showed the effect of age, particularly among younger participants. Specifically, self-reported memory problems were greater among participants younger than 55 years of age. Socioeconomic and racial/ethnic status can affect cancer treatment and its outcomes. However, our analysis revealed that the effects of cancer on CRCD remain after controlling for these variables. These findings call to attention the need to more systematically assess and treat CRCD in patients with cancer and cancer survivors.

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