Title

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Survival Following Dementia Onset: Vascular Dementia versus Alzheimer's Disease

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Summary

Survival following the onset of dementia has been reported to vary from 3 to over 9 years. We examined mortality in 3602 participants of the Cardiovascular Health Cognition Study in four U.S. communities evaluated for dementia incidence between 1992-1999 and followed for 6.5 years. By June 2000, 33 of 62 (53.2%) participants who had developed VaD had died compared to 79 of 245 (32.2%) with AD, 66 of 151 (43.7%) with both AD and VaD, and 429 of 2318 (18.5%) with normal cognition. Using Cox proportional hazards regression with a time-dependent covariate for dementia status adjusted for age, gender and race, individuals with VaD were more than four times as likely to die during follow-up than those with normal cognition (HR: 4.4, 95% CI: 3.1-6.3). The hazard ratios were 2.1 (95% CI: 1.6-2.7) for AD and 2.5 (95% CI: 1.9-3.3) for both types. Adjusted accelerated life models estimated median survival from dementia onset to death as 3.9 years for those with VaD, 7.1 years for AD, and 5.4 years for those with both types of dementia.

Introduction

Although it is generally agreed that the diagnosis of dementia reduces life expectancy, the estimated number of years for survival fol-

lowing the onset of dementia varies. Until recently, the median survival time after dementia was estimated to range from 5 (1) to over 9 years (2). The Canadian Study of Health and Aging, however, reported a median survival of 3.3 years following the onset of dementia (3) using methods to adjust for "length bias" (4), which is reported to overestimate survival because persons with rapidly progressing disease may not be included in the estimates. This type of bias would occur when dementia is assessed at entry into a study and involves those with existing disease at the time. Kawas and Brookmeyer (5) expressed concern that this reduced survival estimate should be interpreted cautiously due to its potential for underestimating the public health burden associated with care of persons with dementia. They emphasized the importance of analyzing survival data from a prospective approach. In the Cardiovascular Health (CHS) Cognition Study, date of onset was determined for dementia cases using prospectively-collected longitudinal data, thus allowing for estimates of survival to be calculated eliminating length bias.

Materials and Methods

The CHS Cognition study utilized data collected from 1989 to 2000 from the Cardiovascular Health Study supplemented with additional measurements of cognition to classify 3,602 individuals for dementia status. The CHS recruited participants from Medicare eligibility lists in four U.S. communities: Forsyth county, NC, Washington county, MD, Sacramento county, CA, and Pittsburgh, PA (6). Methods for both of these studies have been previously reported (7, 8). In brief, CHS participants completed up to ten annual clinic visits at which a vast amount of data were collected including demographics, anthropometry, blood pressure, psychosocial interviews, depression, medical history, health behaviors, physical function, and cognitive function (Modified Mini-Mental State Exam, Digit Symbol Substitution Test, Benton Visual Retention Test). Between 1992-94, cranial magnetic resonance imaging (MRI) was completed on eligible participants. Dementia status of these individuals was classified through the year 2000 using data already collected in the CHS supplemented with additional cognitive measures including neuropsychological testing, if possible. If the participant was deceased or unwilling to come into the clinic, additional data were collected from medical records, physician questionnaires and interviews with the participant or family members (Telephone Interview for Cognitive Status, Neuropsychiatric Inventory, IQCode, and/or Dementia Questionnaire). A committee of neurologists and psychiatrists evaluated all cases of possible dementia and classified each participant for presence and type of dementia using the National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer Disease and Related Disorders Association (NINDS-ADRDA) criteria (9) for Alzheim-

er's disease (AD) and the State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC) criteria (10) for vascular dementia (VaD). Year of onset was determined by review of the longitudinal cognition exams collected in the main study and by family member input collected in the Dementia Questionnaire. Cause of death was classified independently by a separate committee of CHS physicians with expertise in geriatrics. Individuals with prevalent dementia at entry into the cohort and mild cognitive impairment were excluded from these analyses. The Statistical Package for the Social Sciences, version 11.0, and STATA were used to analyze data for this study. Cox proportional hazards regression estimated relative risk of mortality by dementia type compared to those of normal cognition using a time-dependent covariate for dementia status adjusted for age, gender and race. Accelerated life models estimated age-gender-race adjusted median survival time from dementia onset until death.

Results

At entry into the cohort, average age was 75.1 years and participants were followed for an average of 6.5 years. Differences in age, gender, education, comorbidities and ApoE genotype were found by dementia status (Table 1). By June 2000, 33 of 62 (53.2%) participants who had developed VaD had died compared to 79 of 245 (32.2%) with AD, 66 of 151 (43.7%) with both AD and VaD, and 429 of 2318 (18.5%) with normal cognition. Using Cox proportional hazards regression with a time-dependent covariate for dementia status adjusted for age, gender and race (Table 2), individu-

Table 1. Selected characteristics of individuals classified with incident Alzheimer's disease, vascular dementia, or normal cognition after enrollment in the CHS Cognition Study, 1992-3.

Characteristic	Normal Cognition	Alzheimer's disease	Mixed Dementia	Vascular Dementia	p[1]
N	2318	245	151	62	
	N (%) or Mean (sd)	N (%) or Mean (sd)	N (%) or Mean (sd)	N (%) or Mean (sd)	
Mean Age (years)	76.2 (5.2)	80.1 (5.7)	79.8 (6.3)	78.3 (5.2)	<.001
Male Gender	951 (41.0)	83 (33.9)	65 (43.0)	33 (53.2)	.03
Non-White Race	216 (9.3)	42 (17.1)	21 (13.9)	11 (17.7)	<.001
More than High School Education	1190 (51.4)	97 (39.6)	69 (45.7)	25 (40.3)	.001
History of CHD	425 (18.3)	56 (22.9)	39 (25.8)	22 (35.5)	.001
History of Stroke	86 (3.7)	3 (1.2)	20 (13.2)	16 (25.8)	<.001
Hypertension	983 (42.4)	107 (43.7)	81 (53.6)	40 (64.5)	<.001
APOE-4 Allele	465 (21.7)	81 (39.1)	45 (33.8)	11 (19.0)	<.001

1. Chi-square or ANOVA p-value.

Table 2. Associations between all dementia and type of dementia with risk of mortality following onset in 2,776 participants of the CHS Cognition Study.

Dementia Status	Deaths/N	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[1]
Normal Cognition	429/2318	1.0 (reference)	1.0 (reference)
Total Dementia	190/480	3.9 (3.2-4.6)	2.8 (2.3-3.4)
AD Only	79/245	3.0 (2.3-3.8)	2.1 (1.6-2.7)
Mixed Dementia	66/151	3.8 (2.9-4.9)	2.5 (1.9-3.3)
VaD Only	33/62	5.7 (4.0-8.2)	4.4 (3.1-6.3)

1. Adjusted for age at entry into the cohort, gender and race.

als with VaD were more than four times as likely to die during follow-up than those with normal cognitive status (HR: 4.4, 95% CI: 3.1-6.3). The hazard ratios were 2.1 (95% CI: 1.6-2.7) for AD and 2.5 (95% CI: 1.9-3.3) for both types. Cause of death also differed significantly by dementia status (Table 3). Most persons classified with dementia died of causes other than the dementia syndrome itself. Individuals with VaD were more likely to die of cerebrovascular disease (42.4%) than those with AD (8.8%), both types (9.1%) or with normal cognition (7.5%). Those with normal cognition were more likely to die from cancer (40.1%) or coronary heart disease (25.4%) compared to persons with dementia. Accelerated life models adjusted for age, gender and race, estimated median survival from dementia onset to death as 3.9 (3.5-4.2) years for those with VaD only, 7.1 (6.7-7.5) years for those with AD only, and 5.4 (5.2-6.0) years for those with both types of dementia.

Table 3. Cause of death in 607 CHS Cognition Study participants classified with dementia prior to death by dementia type (chi-square p <.001).

Cause of Death	Type of Dementia			
	Normal Cognition	Alzheimer's Disease	Mixed Dementia	Vascular Dementia
Total N Deceased	429	79	66	33
	N (%)	N (%)	N (%)	N (%)
Coronary Heart Disease	109 (25.4)	15 (19.0)	15 (22.7)	4 (12.1)
Cerebrovascular Disease	32 (7.5)	7 (8.8)	6 (9.1)	14 (42.4)
Other Cardiovascular Disease	23 (5.4)	4 (5.1)	2 (3.0)	1 (3.0)
Cancer	172 (40.1)	14 (17.7)	7 (10.6)	3 (9.1)
Dementia/Failure to Thrive	2 (0.5)	15 (19.0)	17 (25.8)	2 (6.1)
Pneumonia/Respiratory	35 (8.1)	6 (7.6)	7 (10.6)	5 (15.1)
Sepsis/Infection	7 (1.6)	4 (5.1)	2 (3.0)	2 (6.1)
Accident/Trauma	14 (3.3)	0 (0.0)	3 (4.6)	0 (0.0)
Other Non-Cardiovascular	35 (8.1)	14 (17.7)	7 (10.6)	2 (6.1)

Conclusion

Estimates of survival using prospectively collected data for date of onset resulted in median survival estimates within the range of those reported by others, but longer than models correcting for length bias. Cause of death and estimated median survival differed by type of dementia. The distribution of dementia type may account for variability found in other investigations of survival following dementia onset.

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