JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 67, NO. 9, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.12.034

ORIGINAL INVESTIGATIONS

Subclinical Cardiovascular Disease and Death, Dementia, and Coronary Heart Disease in Patients 80+ Years

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ABSTRACT

BACKGROUND The successful prevention and treatment of coronary heart disease (CHD) and stroke has resulted in a substantial increase in longevity, with subsequent growth in the population of older people at risk for dementia.

OBJECTIVES The authors evaluated the relationship of coronary and other peripheral atherosclerosis to risk of death, dementia, and CHD in the very elderly. Because the extent of vascular disease differs substantially between men and women, sex- and race-specific analyses were included, with a specific focus on women with low coronary artery calcium (CAC) Agatston scores.

METHODS We evaluated the relationship between measures of subclinical cardiovascular disease (CAC, carotid intimal medial thickness, stenosis, and ankle brachial index) and risk of dementia, CHD, and total mortality in 532 participants of the Cardiovascular Health Study-Cognition Study from 1998/1999 (mean age, 80 years) to 2012/2013 (mean age, 93 years).

RESULTS Thirty-six percent of participants had CAC scores >400. Women and African-Americans had lower CAC scores. Few men had low CAC scores. CAC score and number of coronary calcifications were directly related to age-adjusted total mortality and CHD. The age-specific incidence of dementia was higher than for CHD. Only about 25% of deaths were caused by CHD and 16% by dementia. Approximately 64% of those who died had a prior diagnosis of dementia. White women with low CAC scores had a significantly decreased incidence of dementia.

CONCLUSIONS In subjects 80+ years of age, there is a greater incidence of dementia than of CHD. CAC, as a marker of atherosclerosis, is a determinant of mortality, and risk of CHD and myocardial infarction. White women with low CAC scores had a significantly decreased risk of dementia. A very important unanswered question, especially in the very elderly, is whether prevention of atherosclerosis and its complications is associated with less Alzheimer disease pathology and dementia. (Cardiovascular Health Study [CHS]; NCT00005133) (J Am Coll Cardiol 2016;67:1013-22)

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Manuscript received September 29, 2015; revised manuscript received November 24, 2015, accepted December 14, 2015.

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

ABBREVIATIONS AND ACRONYMS

AA = African American
CAC = coronary artery calcium
CAD = coronary artery disease
CHD = coronary heart disease
CI = confidence interval
CVD = cardiovascular disease
HR = hazard ratio
IMT = intimal medial thickness
MCI = mild cognitive impairment
MI = myocardial infarction
MRI = magnetic resonance imaging
PY = person-years

The prevention and treatment of cardiovascular disease (CVD) has been a primary determinant of increased longevity of older individuals. Improved therapies for clinical coronary heart disease (CHD) and reduced risk factor levels have led to older age at first heart attack, and to higher prevalence of clinical and subclinical CHD (1–5). Women have a lower incidence of clinical CHD than men, even at older ages, and less coronary atherosclerosis, as measured by coronary artery calcium (CAC) (4,6,7). Women also have a first heart attack at an older age than men: at about 72 years of age in women and in the mid-60s in men (8). The extent of subclinical coronary atherosclerosis is a very powerful predictor of risk of clinical coronary artery disease (CAD), congestive heart failure, and stroke (6,9–13). A zero CAC Agatston score is associated with very long-term lower risk of CHD and death, even at older ages (14).

The greater longevity has resulted in an increased population of older people at risk for dementia. Most dementia cases in the United States are older than the age of 75 years at the time of diagnosis. Women live longer than men and, therefore, are at increased lifetime risk for Alzheimer disease, especially at 85+ years of age (15–19). The overall incidence rate of all-cause dementia was similar in men and women in the 90+ study (20). The pathology of dementia at this older age included Alzheimer disease pathology, neurodegeneration, and brain vascular disease (21,22). Numerous studies have documented the association between brain and systemic vascular disease, and risk of dementia (23–31). An important unanswered question is whether older subjects who survived to 80+ years of age with minimal cerebral, peripheral, or coronary atherosclerosis have a reduced risk of dementia and brain neuropathology, as compared with most older patients with extensive subclinical vascular disease.

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Few longitudinal studies have evaluated the relationship between CAC and risk of dementia (31). In the Rotterdam Study, common carotid artery intimal medial thickness (IMT), carotid plaque, and peripheral arterial disease were associated with increased risk of dementia greater than 9 years, attenuated with longer follow-up. The extent of calcification in the coronary arteries, aortic arch, extracranial carotid arteries, and intracranial carotid arteries was correlated cross-sectionally with lower cognitive scores (31–33). Calcification in the intracranial and extracranial carotid arteries (but not coronary artery calcification) was a risk factor for incident dementia. In the Age, Gene/Environmental Susceptibility Study (34), dementia increased with age and was significantly related to quartiles of CAC, reduced by adjustment for other risk factors.

The incidence of dementia (1992 to 1998) was higher in participants with prevalent CVD in a previous report from the Cardiovascular Health Study (CHS). The risk of dementia was higher with increased common and internal carotid IMT, and lower ankle-brachial index (35). Participants with higher CAC scores or greater carotid IMT measurements had more CVD events over 5 years of follow-up (36). Higher CAC scores were associated with more brain magnetic resonance imaging (MRI) vascular abnormalities, and with both mild cognitive impairment (MCI) and prevalent dementia, but not after age adjustment (37,38). Black persons had lower CAC than white persons (39).

In this study, we examined the relationship of subclinical CAD and risk of clinical CVD and dementia at 80+ years of age in 532 participants of the CHS Cognition Study (CHS-CS) in Pittsburgh from 1998/1999 to 2014. We specifically tested 2 hypotheses in participants aged 80+ years followed for 10+ years: whether CAC and other measures of subclinical vascular disease predict risk of death and risk of dementia and CHD. We further evaluated whether these associations were similar among men and women.

This report differs from previous CHS publications that included CAC by including predominantly older-age participants 80+ years of age, much longer follow-up, more detailed evaluations of dementia status, and incident (as compared with predominantly prevalent) dementia.

METHODS

The CHS-CS dementia follow-up study was a continuation of the original CHS limited to the Pittsburgh field center of the CHS from 1998/1999 to 2014. In 1992 to 1994, a total of 924 participants had an MRI of the brain. In 1998/1999, 532 of the 924 (58%) participants were included in the Pittsburgh CHS-CS (1998/1999 through 2014) if alive and not demented in 1998/1999, and having either a second MRI and/or a detailed cognitive evaluation in 1998/1999 (40,41). There were 199 deaths and 116 demented before 1998/1999 and, of the 609 participants eligible for the Pittsburgh CHS-CS, 87.5% (n = 532) were included in the study: 449 who had a second MRI and 83 with detailed cognitive evaluation only. The 77 eligible participants not included in the detailed study were followed as part of the CHS, but did