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Investigating the Associations of Cardiovascular Risk Factors, Conditions, and Interventions with Cerebrovascular Diseases: The 90+ study

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Abstract

Background: In the oldest-old (those >90 years) cerebrovascular diseases are highly prevalent and independently associated with dementia. Although cardiovascular risk factors like hypertension (HTN), hyperlipidemia (HLD), and diabetes mellitus (DM) are thought to be major contributors to the development of cerebrovascular diseases, autopsy studies in the oldest-old show weak associations with HTN, no association with DM, and HLD remains understudied. We expanded upon existing studies by investigating the associations of cardiovascular risk factors, conditions, interventions, and APOE genotype with the presence of cerebrovascular diseases in participants >90-years-old.

Methods: Participants are from The 90+ study, a population-based epidemiology study of dementia and aging whose participants were survivors of the Leisure World cohort (n = 267). The self-reported cardiovascular risk factors were DM, HLD, and HTN. Cardiovascular conditions were arrhythmia, coronary artery disease, congestive heart failure (CHF), heart valve disease, myocardial infarction, stroke, and transient ischemic attack. Cardiovascular interventions were coronary artery bypass, pacemaker placement, and statin use. Cerebrovascular diseases were arteriolosclerosis, atherosclerosis, cerebral amyloid angiopathy (CAA), and microvascular lesions (MVLs) on autopsy. Neuropathologic evaluation followed NIA-AA guidelines. We investigated the association between individual cardiovascular risk factors, conditions, interventions, and APOE genotype with individual cerebrovascular pathologies using logistic regressions adjusted for age of death, sex, and education.

Results: Participants were on average 98.1 years at death and 75% were female (Table 1). None of the cardiovascular features were associated with arteriolosclerosis or atherosclerosis (Figure 1). APOE-ε4 was positively associated with CAA [OR = 3.62] while DM [OR = 0.23] and statin use [OR = 0.57] were negatively associated (Figure 2). CHF was negatively associated with the likelihood of MVLs [OR = 0.39] (figure 2).

Conclusions: Cardiovascular risk factors were not associated with cerebrovascular pathologies in our age group, leading to three potential interpretations: 1) they are not risk factors for cerebrovascular pathologies, 2) they have been mitigated through

treatment, or 3) they are not associated due to survival bias, as these conditions reduce life expectancy. Associations of APOE-ε4, DM, and statin use with CAA may relate to β-amyloid metabolism while CHF's negative association with MVLs may relate to decreased blood pressure variability. These initial findings on the limited associations warrant further exploration.

Table 1. Participant Characteristics (N=267).

Characteristic	N (%)
Female sex,	201 (73.5)
College education or higher	127 (47.6)
Dementia at last visit	133 (50.2)
Vascular Neuropathologic Changes	
Arteriolosclerosis (mild, moderate, severe)	217 (81.3)
Atherosclerosis (mild, moderate, severe)	207 (78.4)
CAA (mild, moderate, severe)	135 (50.6)
MVL (≥1)	73 (27.3)
Cardiovascular Risk Factors (Self-reported)	
DM	16 (6.0)
HLD	93 (34.8)
HTN	156 (58.6)
Cardiac conditions (Self-reported)	
Arrhythmia	94 (35.9)
CAD	48 (18.3)
CHF	55 (20.8)
Heart Disease	153 (57.5)
HVD	26 (9.9)
MI	37 (14.0)
Stroke	40 (15.4)
TIA	73 (28.9)
Cardiac Interventions (Self-reported)	
CAB	16 (6.1)
Pacemaker placement	41 (15.6)
Statin use	78 (29.2)
APOE status	
APOE-e2 allele	36 (13.5)
APOE-e4 allele	53 (20.6)

CAA=cerebral amyloid angiopathy. CAB= coronary artery bypass. CAD=coronary artery disease. CHF=congestive heart failure. DM= diabetes mellitus. Heart disease=composite variable of arrhythmia, CAB, CAD, CHF, HVD, and MI. HLD= hyperlipidemia. HTN=hypertension. HVD= heart valve disease. MI=myocardial infarction. MVL=microvascular lesions. TIA=transient ischemic attack.

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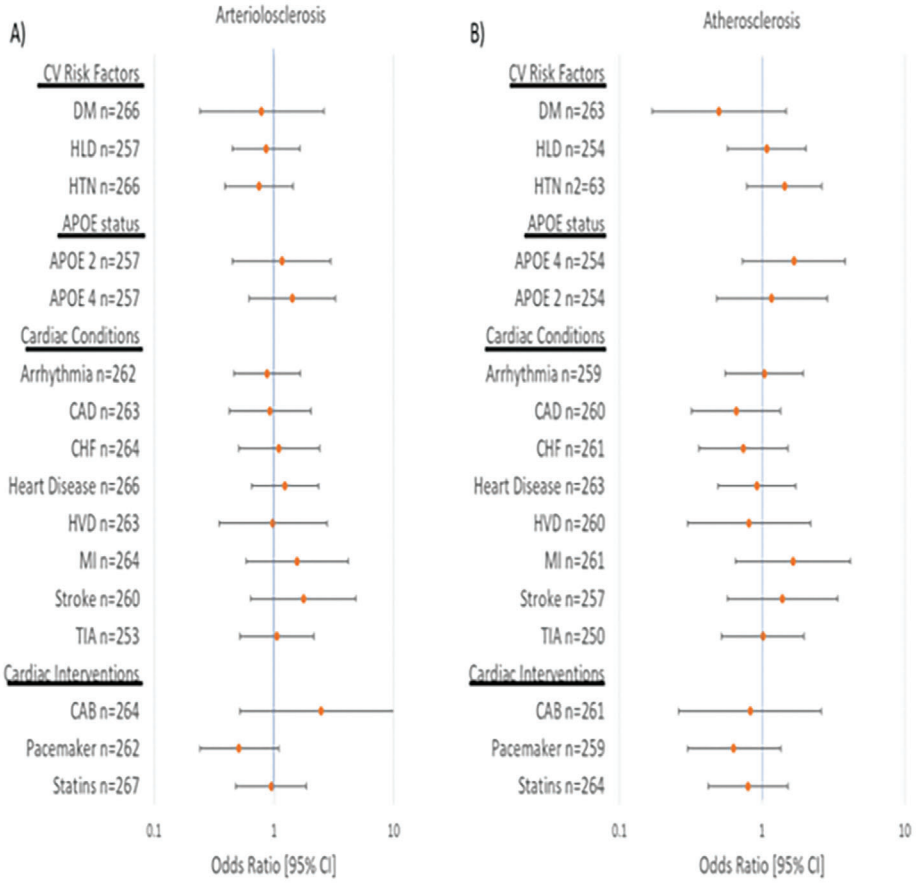
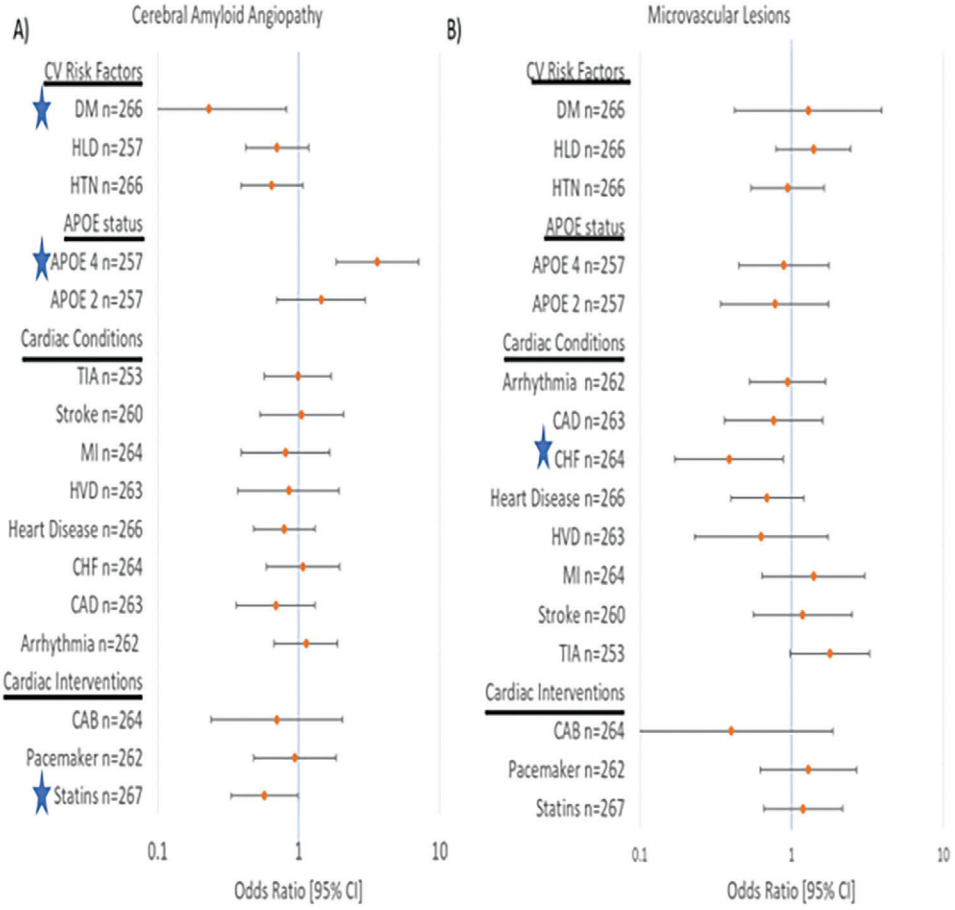
Figure 1. Odds ratios for the likelihood of the presence of a) arteriolosclerosis and b) atherosclerosis by cardiovascular risk factor, condition, intervention, and APOE status.



APOE= apolipoprotein E gene. CAB=coronary artery bypass. CAD=coronary artery disease. CHF=congestive heart failure. CV=cardiovascular. DM=diabetes mellitus. HLD=hyperlipidemia. HVD= heart valve disease. HTN=hypertension. MI=myocardial infarction. TIA=transient ischemic attack. Odds ratios from individual logistic regression models adjusted for age of death, sex, and education.

Figure 2. Odds ratios for the likelihood of the presence of a) cerebral amyloid angiopathy and b) microvascular lesions by self-reported cardiovascular risk factors adjusted for age of death, sex, and education.



APOE= apolipoprotein E gene. CAB=coronary artery bypass. CAD=coronary artery disease. CHF=congestive heart failure. DM=diabetes mellitus. HLD=hyperlipidemia. HVD= heart valve disease. HTN=hypertension. MI=myocardial infarction. TIA=transient ischemic attack. ★ p-value <0.05. Odds ratios from individual logistic regression models adjusted for age of death, sex, and education.