UC Irvine
UC Irvine Previously Published Works

Title

Associations of Cardiovascular Risk Factors and Cerebrovascular Pathologies in the Elderly: A Systematic Review

Permalink

Journal

ISSN

Authors

Wong, Joey
Rajmohan, Ravi
Corrada, María MM
et al.

Publication Date

DOI

Copyright Information

Peer reviewed

BASIC SCIENCE AND PATHOGENESIS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

HUMAN NEUROPATHOLOGY

Associations of Cardiovascular Risk Factors and Cerebrovascular Pathologies in the Elderly: A Systematic Review

Joey Wong | Ravi Rajmohan | María M. M. Corrada | Claudia H. Kawas

University of California, Irvine, Irvine, CA, USA

Correspondence
Joey Wong, University of California, Irvine,
Irvine, CA, USA.
Email: wongjy2@hs.uci.edu

Abstract

Background: Cerebrovascular pathologies are common in the elderly and are associated with dementia. Cardiovascular risk factors are thought to contribute to their development, but this evidence mainly comes from imaging studies or autopsy studies in younger individuals. We performed a systematic review to investigate associations of cardiovascular risk factors with cerebrovascular pathologies in the oldest-old (age >80) vs. the younger-old (ages 65-80).

Methods: Figure 1 describes how studies were identified. Cardiovascular risk factors were hypertension (HTN), hyperlipidemia (HLD), and diabetes (DM). Cerebrovascular pathologies were arteriolosclerosis, atherosclerosis, CAA, and MVLs. PubMed, Scopus, and Web of Science databases were searched for articles in English that investigated associations between self-reported cardiovascular risk factors and presence of cerebrovascular pathologies on autopsy with a mean age >65 years, which reported odds ratios (OR), or information to calculate OR, for the individual associations of cardiovascular risk factors and cerebrovascular pathologies. Initial searching involved all combinations of cardiovascular MeSH terms by cerebrovascular pathology MeSH terms (n = 1038). JW and RR screened titles and abstracts to identify potential studies (n = 45), which reduced to 10 after applying the restrictions above. We used meta-analytic methods to estimate OR when multiple studies reported on the same associations.

Results: We reviewed 10 studies (Table 1) from 6 unique cohorts (n = 1,815, ages 65-80 and n = 7,995, age >80). HTN was positively associated with cerebrovascular pathologies for all the instances except arteriolosclerosis-oldest-old [OR = 1.20, n = 2,089], (arteriolosclerosis-younger-old [OR = 1.30 n = 1,599], atherosclerosis-oldest-old [OR = 1.29, n = 2,620], CAA-oldest-old [OR = 1.23, n = 2,198], and MVLs-oldest-old [OR = 1.54, n = 1,710]) (Figure 2). HLD was associated with arteriolosclerosis in the younger-old ([OR = 1.27 n = 922]), but not the oldest-old ([OR = 0.98, n = 1,255]), and not associated with CAA in the oldest-old ([OR = 1.13, n = 3,508]). DM was not associated in any situation in which it was investigated (Figure 2).

Conclusions: Cardiovascular risk factors were more associated with cerebrovascular pathologies in the younger-old than oldest-old. HTN was consistently associated with cerebrovascular pathologies in both age groups while DM was consistently not associated. Cardiovascular risk factors were understudied in the younger-old. These findings highlight the importance of further clinicopathologic studies to clarify age-dependent associations of cardiovascular risk factors and cerebrovascular pathologies.
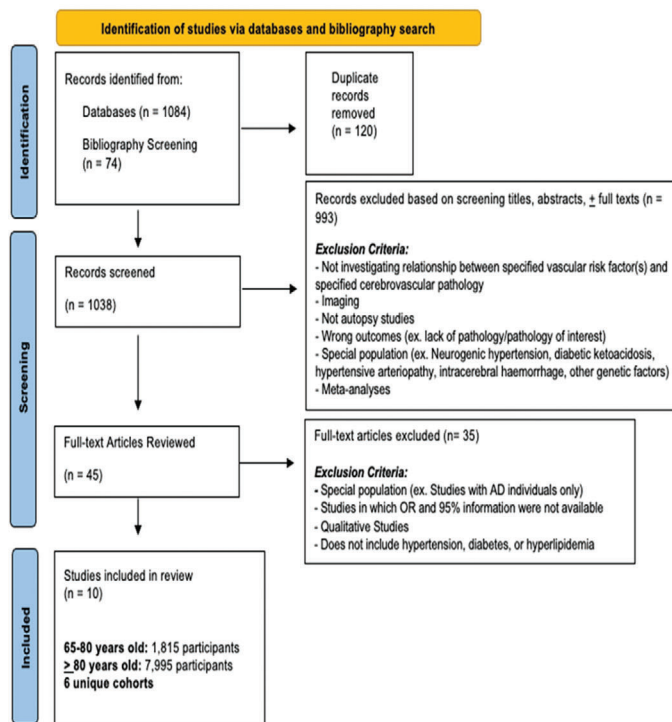
Figure 1: Description of data extraction for identification of studies

- MeSH terms used as keywords to search for independent variables (cardiovascular risk factors)- "Hypertension", "Diabetes Mellitus", "Hypercholesterolemia", "Hyperlipidemia".
- MeSH terms used as keywords to search for dependent variables (cerebrovascular pathology)- "arteriolosclerosis", "atherosclerosis, cerebral", "cerebral amyloid angiopathy", "microvascular, cerebral"
- A matrix of the association between independent variables (cardiovascular risk factors) and dependent variables (cerebrovascular pathology) (for example, Hypertension[MeSH Terms] AND arteriolosclerosis[MeSH Terms]) was used. Additional filters limited results to studies published involving humans, that were in English, and with full text files available. This identified 1,038 results, which was reduced to 45 potential articles by review of titles and abstracts for relevance. Further screening led to the identification of 10 unique studies that explicitly looked at associations between cardiovascular risk factors and cerebrovascular pathologies findings on autopsy from 6 unique cohorts. Studies that did not provide information from which odds ratios for the association between the presence of cardiovascular risk factors and the presence of cerebrovascular pathologies could be calculated were excluded.

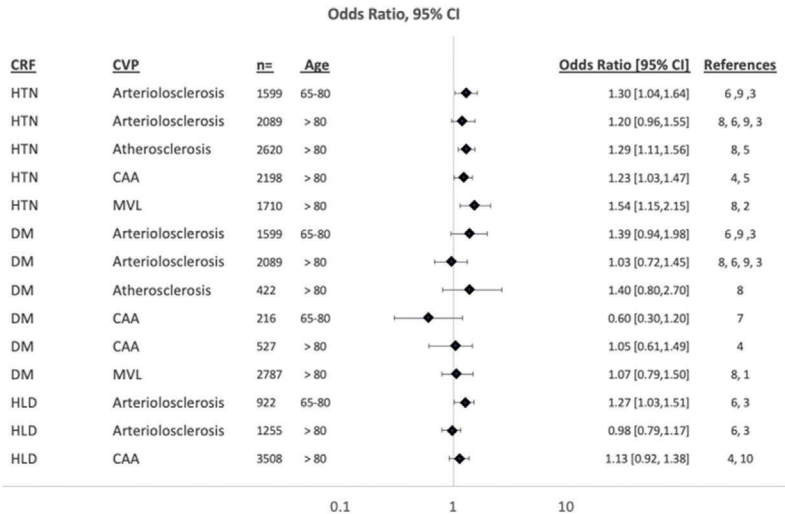| Reference	Independent variable(s)	Dependent variable(s)	Age 65-80	Age >80	n	Cohort
Blevins 2021 [3]	HTN/HLD/DM	Arteriolo	<80		762	NACC NP v10 Data, 6/2014-3/2020
Blevins, 2021 [3]	HTN/HLD/DM	Arteriolo		>80	1361	NACC NP v10 Data, 6/2014-3/2020
Ighodaro 2017 [6]	HTN/HLD/DM	Arteriolo	70 (6)		922	NACC and ADNI data sets
Ighodaro, 2017 [6]	HTN/HLD/DM	Arteriolo		88 (4)	1255	NACC and ADNI data sets
Richardson, 2012 [8]	HTN/DM	Arteriolo/Athero/MVL		87 (7)	422	MRC CFAS
Suemoto, 2019 [9]	HTN/DM	Arteriolo	67.0 (8.9)		677	BB-BABSG
Suemoto, 2019 [9]	HTN/DM	Arteriolo		85.7 (4.7)	412	BB-BABSG
Eglit, 2020 [5]	HTN	Athero/CAA		84 (10)	2198	NACC UDS and NP Data Set
Brenowitz, 2015 [4]	HTN/HLD/DM	CAA		83.2 (8)	527	NACC MDS, UDS, NP Data Set
Arvanitakis, 2018 [2]	HTN	MVL		88.6 (6.7)	1288	RUSH AD Center Community Based Cohort
Xu, 2020 [10]	HLD	CAA		80.4 (11.8)	3508	NACC 2005- 2017
Peila, 2002 [7]	DM	CAA	77.0 (4.1)		216	HAAS
Abner, 2016 [1]	DM	MVL		88.7 (6.5)	2365	SMART

References: [PMID] 1. Abner, 26812281; 2. Arvanitakis, 29997190; 3. Blevins, 33098484; 4. Brenowitz, 26239176; 5. Eglit, 33543127; 6. Ighodaro, 26738751; 7. Peila, 11916953; 8. Richardson, 22471870; 9. Suemoto, 30861605; 10. Xu, 31929164.

<u>Table 1. Unique Studies and Summary of Results</u>.
A) Description of unique studies. ADNI= Alzheimer's Disease Neuroimaging Initiative, APOE=apolipoprotein E, Arteriolo=arteriolosclerosis, Athero=atherosclerosis, BB-BABSG=Brain Bank of the Brazilian Aging Brain Study Group, CAA=cerebral amyloid angiopathy, DM=diabetes mellitus, HAAS= Honolulu Asia Aging Study, HLD=hyperlipidemia, HTN=hypertension, MDS= Minimum Data Set, MRC CFAS= Medical Research Council Cognitive Function and Ageing Study, NACC=National Alzheimer's Coordinating Center, NP v10= Neuropathology version 10, SMART= Statistical Modeling of Aging and Risk of Transition Project, UDS=Uniform Data Set.

Figure 2: Odd ratios for associations of cardiovascular risk factors: cerebrovascular pathologies.

A) Forest plot of odds ratios.
CAA=cerebral amyloid angiopathy,
CI=confidence intervals,
DM=diabetes mellitus,
HLD=hyperlipidemia,
HTN=hypertension,
MVL=microvascular lesions.

Odds Ratio, 95% CI

CRF	CVP	n=	Age	Odds Ratio [95% CI]	References
HTN	Arteriolosclerosis	1599	65-80	1.30 [1.04,1.64]	6, 9, 3
HTN	Arteriolosclerosis	2089	>80	1.20 [0.96,1.55]	8, 6, 9, 3
HTN	Atherosclerosis	2620	>80	1.29 [1.11,1.56]	8, 5
HTN	CAA	2198	>80	1.23 [1.03,1.47]	4, 5
HTN	MVL	1710	>80	1.54 [1.15,2.15]	8, 2
DM	Arteriolosclerosis	1599	65-80	1.39 [0.94,1.98]	6, 9, 3
DM	Arteriolosclerosis	2089	>80	1.03 [0.72,1.45]	8, 6, 9, 3
DM	Atherosclerosis	422	>80	1.40 [0.80,2.70]	8
DM	CAA	216	65-80	0.60 [0.30,1.20]	7
DM	CAA	527	>80	1.05 [0.61,1.49]	4
DM	MVL	2787	>80	1.07 [0.79,1.50]	8, 1
HLD	Arteriolosclerosis	922	65-80	1.27 [1.03,1.51]	6, 3
HLD	Arteriolosclerosis	1255	>80	0.98 [0.79,1.17]	6, 3
HLD	CAA	3508	>80	1.13 [0.92, 1.38]	4, 10

0.1   1   10

B) Summary of results.
"+" = positive association,
"-" = negative association,
"0" = no association,
"?" = no studies identified investigating this association.

	Arteriolo		Athero		CAA		MVL	
	65-80	>80	65-80	>80	65-80	>80	65-80	>80
HTN	+	0	?	+	?	+	?	+
HLD	+	0	?	?	?	0	?	?
DM	0	0	?	0	0	0	?	0