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Short Communication

Vascular risk factor burden and new-onset depression in the community

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ABSTRACT

Depression is associated with an increased likelihood of cardiac events and stroke. We hypothesized that the vascular risk factor burden might itself predispose to both cardiovascular events and depression. Therefore, we examined whether aggregate scores of vascular risk factor burden were associated with the new-onset of depression in the community. We studied 2023 depression- and dementia-free Framingham Heart Study (Framingham, USA) Offspring participants who attended both examination cycles 7 (1998–2001) and 8 (2005–2008). The American Heart Association Ideal Cardiovascular Health metric and the Framingham stroke risk profile were calculated at exam seven. New-onset depression was adjudicated at examination cycle eight as antidepressant medication use or Centre for Epidemiologic Studies Depression Scale scores ≥ 16, after a mean follow-up of 6.6 years (standard deviation = 0.7). Of the 2023 participants, 269 (13%) developed new-onset depression. Following adjustments for age, sex, education, and the time interval between baseline and follow-up, the odds of new-onset depression decreased by 10% for each one-point increase in ideal cardiovascular health scores (Odds Ratio [OR], 0.90; 95% confidence interval [CI] 0.81–0.99) and increased by 4% for each percentage point increase in the Framingham stroke risk profile (OR, 1.04; CI, 1.00–1.07). Results were not explained by interim clinical stroke or cerebral white matter injury. In conclusion, vascular risk factor burden was associated with the new onset of depression. Shared vascular risk factors may contribute to the increased risk of cardiovascular events observed in persons with depression.

1. Introduction

Depression and cardiovascular disease are leading causes of disability in the developed world (Kassebaum et al., 2016). Evidence suggests that depression and cardiovascular disease may share a bi-directional relationship. Vulnerability to both conditions may be due to shared genetic or environmental risk factors; Depression is associated with an increased likelihood of cardiac events and stroke, presumably because of its association with vascular risk factors such as smoking, obesity, physical inactivity, poor diet, and shared genetic factors (Xian et al., 2010; Penninx, 2017; Dong et al., 2012; Kendler et al., 2009). We hypothesized that vascular risk factor burden might also predispose to the risk of new-onset depression, thereby establishing common factors underlying both risks for cardiovascular disease and depression.

The ideal-cardiovascular health metric was developed as part of the American Heart Association's 2020 impact goals (Lloyd-Jones et al., 2010). The metric awards one point for meeting each recommended target for four health behaviors (non-smoking, body mass index, physical activity, and diet) and three risk factors (serum total cholesterol, blood pressure, and fasting blood glucose) with a score of seven reflecting ideal-cardiovascular health. We recently demonstrated that higher ideal-cardiovascular health scores were associated with a lower risk of incident cardiovascular disease, stroke, dementia, brain atrophy and cognitive decline (Pase et al., 2016; Xanthakis et al., 2014). In our previous study, each point higher ideal-cardiovascular health scores was associated with a 20% lower chance of stroke within ten years among participants of the Framingham Heart Study (Pase et al., 2016). The Framingham stroke risk profile is a widely used algorithm to

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; OR, odds ratio

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estimate the 10-year risk of stroke based on clinical information (Dufouil et al., 2017).

The aim of the present study was to examine the prospective association between overall vascular risk factor burden, using the ideal-cardiovascular health and Framingham stroke risk profile metrics, and new-onset depression in participants of the community-based Framingham Heart Study.

2. Methods

The Framingham Heart Study Offspring cohort commenced in 1971 with the enrollment of 5124 volunteers (Feinleib et al., 1975). Participants have been studied across 9 examination cycles, once approximately every four years. Between 1998 and 2001, 3539 Offspring participants attended the seventh Heart Study examination cycle. Using these data as a baseline, we captured ideal-cardiovascular health and Framingham stroke risk profile scores for 2750 participants. We excluded 372 participants who were deemed to be depressed at baseline based on the use of antidepressants or a Center for Epidemiologic Studies Depression Scale (CES-D) score ≥ 16, and 6 participants with prevalent dementia. Of the remaining 2372 participants, our analysis sample included 2023 persons who returned for follow-up at the eighth heart study examination cycle (2005–2008) and had complete data on medication use and CES-D scores. All participants provided written informed consent, and the study was approved by the Institutional Review Board and Boston University Medical Center.

2.1. Assessment of vascular risk

Consistent with our previous work (Pase et al., 2016; Xanthakis et al., 2014), the ideal-cardiovascular health score was operationalized by awarding one point for each of the following; never smoked or quit > 12 months ago, body mass index < 25 kg/m^2, adequate physical activity (≥ 150 min/week moderate intensity or ≥ 75 min/week vigorous intensity or a combination of the two), a healthy diet (≥ 2 of the following components: > 4.5 cups/day fruits and vegetables, ≥ 2 × 3.5 oz. servings/week of fish, ≥ 3 × 1 oz. servings/day of fiber-rich whole grains, < 1500 mg/d of sodium, & ≤ 36 oz./week of sugar-sweetened beverages), serum total cholesterol untreated and < 200 mg/dL, blood pressure untreated and < 120/ < 80 mm Hg (measured twice by a physician with results averaged), and fasting plasma glucose untreated < 100 mg/dL. Diet and physical activity were measured with the use of a validated Harvard semi-quantitative food frequency (Rimm et al., 1992) and physical activity index questionnaire (Kannel & Sorlie, 1979), respectively, whereas all other variables were obtained from the Framingham Heart Study clinic. Smoking status was assessed in a clinical interview. Blood pressure was measured by a physician using a mercury sphygmomanometer with the participant supine and following 5 min rest. Fasting cholesterol was measured in 99% of our sample. We calculated the recently updated Framingham stroke risk profile according to published criteria (Dufouil et al., 2017). The algorithm combines information on age, current smoking status, prevalent cardiovascular disease, prevalent atrial fibrillation, diabetes, hypertension treatment and systolic blood pressure. This updated algorithm has been validated in 3 large community samples (Dufouil et al., 2017). Higher Framingham stroke risk profile scores indicate a higher risk of incident stroke.

2.2. Assessment of new-onset depression

New-onset depression was defined at examination cycle eight as the use of antidepressants or CES-D scores ≥ 16. This CES-D threshold has been shown to have high sensitivity and specificity for detecting major depression in community-dwelling older adults (Beekman et al., 1997).

2.3. Statistical analysis

We used logistic regression models to relate continuous ideal-cardiovascular health and Framingham stroke risk profile scores at examination cycle seven to the new onset of depression at examination cycle eight (mean follow-up of 6.6 years, SD 0.7). Results are expressed as odds ratios (OR) and 95% confidence intervals (CI) and are adjusted for age, sex, education and the time interval between baseline and follow-up.

We performed sensitivity analysis to examine whether any associations between vascular risk and new-onset depression could be explained by clinical stroke or silent cerebral small vessel disease. Therefore, we included additional adjustments for prevalent stroke (n = 25) at baseline and as well as prevalent stroke combined with interim stroke between baseline and follow-up (n = 51). Next, we examined mediation by white matter hyperintensity volume, which was quantified at a date proximal to baseline using a Siemens 1 T or 1.5 T field strength machine with a T2-weighted double spin-echo coronal imaging sequence in contiguous slices of 4 mm (DeCarli et al., 2005). Values of white matter hyperintensity volume were expressed as a percentage of intracranial volume and were log transformed. Lastly, we examined the association between vascular risk and the onset of depressive symptoms, defined solely by CES-D scores ≥ 16 in participants who were not using antidepressants (participants taking antidepressants were excluded from analysis). Results were considered significant if $p < 0.05$.

3. Results

Cohort demographics are summarized in Table 1 with results displayed in Table 2. The age range of participants was from 37 to 88 years. Of the 2023 participants, 269 (13%) developed new-onset depression at follow-up. The odds of new-onset depression decreased by 10% for each one-point increase in ideal-cardiovascular health scores. Each percentage point increase in the Framingham stroke risk profile was associated with 4% higher odds of new-onset depression. Effect sizes were similar when examining the association between vascular risk and the new onset of depressive symptoms (after excluding persons taking antidepressants). Effect sizes were also comparable after additional adjustment for prevalent stroke at baseline as well as both prevalent and interim stroke. White matter hyperintensity volume was not associated with new-onset depression (Odds Ratio, 1.03; 95% confidence interval, 0.88–1.22) and was not considered to be a potential mediator.

Table 1
Characteristics of the study sample at baseline.

	Sample mean (SD)[a]
Age, years	61 (9)
Men, n (%)	946 (47)
Education, n (%)	
No high school	68 (3)
High-school degree	1124 (57)
College graduate	790 (40)
Body mass index, kg/m^2, median [Q1, Q3]	27 [24, 31]
Systolic blood pressure, mm Hg	126 (18)
Hypertension treatment, n (%)	638 (32)
Total cholesterol, mg/dL	201.0 (35.9)
High density lipoprotein cholesterol, mg/dL	53.8 (16.6)
Prevalent diabetes, n (%)	185 (9)
Prevalent atrial fibrillation, n (%)	65 (3)
Prevalent cardiovascular disease, n (%)	211 (10)
CES-D, score units, median [Q1, Q3]	3 [1, 5]
Ideal-cardiovascular health, score units	3 (1)
Framingham stroke risk profile, %, median [Q1, Q3]	2 [1, 5]

[a] Unless specified otherwise. CES-D - Center for Epidemiologic Studies Depression Scale.

Table 2
Association of vascular risk factor burden and new-onset depression.

Predictor	Risk for new-onset depression[a]	Risk for new-onset depressive symptoms[b]
	OR (95% CI)	OR (95% CI)
Basic model		
Ideal-cardiovascular health	0.90 (0.81, 0.99)	0.84 (0.71, 0.99)
Framingham stroke risk profile	1.04 (1.00, 1.07)	1.06 (1.00, 1.12)
Basic model plus adjustment for prevalent stroke		
Ideal-cardiovascular health	0.90 (0.81, 0.99)	0.84 (0.71, 0.99)
Framingham stroke risk profile	1.04 (1.00, 1.07)	1.06 (1.01, 1.12)
Basic model plus adjustment for prevalent and interim stroke		
Ideal-cardiovascular health	0.90 (0.81, 0.99)	0.84 (0.71, 0.99)
Framingham stroke risk profile	1.03 (1.00, 1.07)	1.06 (1.00, 1.11)

All models are adjusted for age, sex, education and the time interval between baseline and follow-up.

[a] Defined as CES-D scores ≥ 16 or antidepressant use. After adjustment for covariates, the sample size was 1982 with 264 events.

[b] Defined as CES-D scores ≥ 16 with antidepressant users excluded from analysis. After adjustment for covariates, the sample size was 1192 with 92 events.

4. Discussion

Our large prospective population-based study demonstrates that higher ideal-cardiovascular health and lower Framingham stroke risk profile scores were associated with a lower odds of new-onset depression, as defined by new antidepressant use or the development of significant depressive symptomatology. Results were similar after adjustments for clinical stroke and were not accounted for by subclinical white matter injury. Collectively, our results suggested that vascular risk factor burden is associated with new-onset depression across the adult age range, independent of overt stroke and subclinical white matter disease.

Whereas vascular risk factors have been hypothesized to underlie the association between prevalent depression and cardiovascular events (Penninx, 2017), our results suggest that the adherence to simple cardiovascular health targets was associated with a lower risk of developing depression in the first instance. This suggests that the association between depression and cardiovascular disease may be due to shared vascular risk factor burden. Our findings also extend our previous findings demonstrating that higher ideal-cardiovascular health scores were associated with a lower risk of incident cardiovascular disease, stroke, dementia, brain atrophy and cognitive decline (Pase et al., 2016; Xanthakis et al., 2014). Further research is warranted to determine whether improving cardiovascular health lowers the risk of developing depression. This is an important topic because further promotion of heart-healthy guidelines, such as the ideal-CVH guidelines, may help lower the burden of cardiovascular disease and depression in the community.

The present study was not without limitations. The sample was comprised mostly of Caucasians, thereby limiting the generalizability of our findings to other ethnic groups. The associations between vascular risk factor burden and new-onset depression could not be explained by overt stroke or white matter hyperintensities. However, we cannot exclude the possibility that more subtle cerebrovascular disease (undetectable by our imaging methods) was responsible for the observed associations. More sensitive imaging measures of white matter integrity such as fractional anisotropy or free water diffusion will be required to explore this further. Further understanding the mechanisms linking vascular risk to new-onset depression may help clarify whether reducing cardiovascular disease risk can mitigate the risk of depression. Moreover, we did not have data on current or previous psychiatric disorders to include in our analysis. Lastly, new-onset depression was defined according to CES-D scores or medication use, rather than a physician diagnosis of clinical depression. It is possible that some participants, not captured as being depressed at baseline, may have had depression earlier in life.

In summary, vascular risk factor burden was associated with the new-onset of depression. Further research is warranted to replicate our findings and to evaluate whether reducing vascular risk factors attenuates the risk of developing depression.

Transparency document

The Transparency document associated with this article can be found, in online version.

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Conflict of interest

All other authors report no disclosures or potential conflicts of interest.

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