Vascular Burden and Cognitive Function in Late-Life Depression

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Objective: *To evaluate the relation of vascular risk factors, subclinical, and manifest vascular disease with four domains of cognitive functioning in a large sample of clinically depressed older persons.* **Methods:** *A cross-sectional analysis was used, and depressed patients were recruited from general practices and mental healthcare institutes. Presence of a* Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, *depressive episode was established with the Composite International Diagnostic Interview. Framingham Risk Score (FRS) was used as a measure for vascular risk profile, ankle-brachial index for subclinical vascular disease, and history of a cardiovascular event as a measure for manifest vascular disease. Three neurocognitive tasks evaluated processing speed, working memory, verbal memory, and interference control.* **Results:** *In 378 participants, linear regression analysis showed that FRS was related to poorer interference control ($t = -2.353$; $df = 377$; $p < 0.05$) but to no other cognitive domain after adjustment for age, sex, education level, and depressive symptom severity. Lower ankle-brachial index and history of cardiovascular event were related to slower processing speed ($t = 2.659$; $df = 377$; $p < 0.05$ and $t = -3.328$; $df = 377$; $p < 0.01$, respectively) but to no other cognitive domain. In 267 participants without manifest vascular disease, higher FRS was related to slower processing speed ($t = -2.425$; $df = 266$; $p < 0.05$) and poorer interference control ($t = -2.423$; $df = 266$; $p < 0.05$), and lower ankle brachial index was related to slower processing speed ($t = 2.171$; $df = 266$; $p < 0.05$).* **Conclusion:** *In depressed older persons, vascular burden is related to slower processing speed also in the absence of manifest vascular disease. Poorer interference control was only related to vascular risk factors but not to subclinical or manifest vascular disease.* (Am J Geriatr Psychiatry 2014; ■:■−■)

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INTRODUCTION

Vascular burden is thought to be involved in cognitive decline and development of dementia.[1] Measures of subclinical vascular disease, including carotid intima media thickness and ankle-brachial index, are associated with poorer cognitive functioning and cognitive decline.[2,3] Also, cardiovascular risk factors, including hypertension, diabetes, obesity, and hypercholesterolemia, are associated with poorer cognitive functioning.[4,5] These findings suggest that proper cardiovascular risk reduction and prevention strategies may prevent or postpone cognitive decline.

Although the relation between vascular burden and cognitive functioning is well studied in older persons from the general population, it is less well studied in depressed older persons. Because depression itself is strongly related to poorer cognitive functioning and decline,[6] it remains unclear whether vascular burden also relates to poorer cognitive functioning in depressed older persons. Depression is related with poorer health behaviors, noncompliance to treatments, noncompliance to cardiac aftercare regimens, and even less optimal cardiac care.[7–10] Therefore, if vascular burden affects cognitive functioning and development of dementia in depressed older persons, it is essential to improve proper cardiovascular care and risk factor modification in this patient group.

Only a few studies evaluated the impact of vascular burden on cognitive functioning in depressed older persons. Three studies evaluated the impact of a composite vascular risk score originally developed to predict 10-year risk of stroke on cognitive function, independent of depressive symptom severity.[11–13] One study found this composite score to relate to slower processing speed but not to other cognitive domains.[11] The second found the composite score to relate to poor attention and cognitive control but not verbal fluency and memory.[13] The third study found no relation of this composite score with processing speed, attention, working memory, episodic memory, and speed of memory.[12] In a fourth study, subclinical vascular disease, particularly flow-mediated dilation, related to poor working memory and executive functioning but not verbal memory.[14] These studies used small samples of patients (41–198) in relatively good physical health limiting generalization to depressed older persons in general.

The present study evaluated the association between vascular burden and cognitive functioning in a large and representative sample of depressed older persons. To elucidate during which stage of the cardiovascular disease process cognitive functioning may become affected, a distinction is made between vascular risk factors, subclinical vascular disease, and manifest vascular disease.

METHODS

Study Design and Sample

The Netherlands Study of Depression in Older Persons is a multisite naturalistic cohort study of depressed older persons in whom vascular burden and cognitive functioning were extensively measured.[15] Between 2007 and 2010, 378 participants were recruited from both mental healthcare institutes (N = 326) and general practices (N = 52) in five regions in the Netherlands.

Inclusion criteria were age ≥60 years and the presence of a *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* depressive disorder established with a structured diagnostic interview.[16] Exclusion criteria were a primary diagnosis of dementia, suspicion of dementia according to the general practitioner as well as after a psychiatric diagnostic work-up by an old-age psychiatrist, a Mini-Mental State Exam (MMSE) Score under 18, severe mental illness or severe physical or cognitive frailty limiting participation, and insufficient command of the Dutch language.

General practitioners referred participants scoring either ≥4 on the Geriatric Depression Scale (N = 35) or with depressive complaints (N = 17). Of 242 screen-positive participants (Geriatric Depression Scale ≥4) 184 were not eligible (76.0%). Of the remaining 58 eligible patients, 23 (39.7%) refused to participate, leaving 35 participating individuals. Response and eligibility rates were not available for the 17 participants referred by general practitioners because of depressive complaints. From mental healthcare institutes, response rates were only available for one site (Amsterdam) but are likely representative for the