Cardiovascular Health and Cognitive Decline 2 Decades Later in Men with Preexisting Coronary Artery Disease

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Cardiovascular health (CVH) factors are associated with lower risk of cardiovascular disease, stroke, and mortality. We investigated the association between a modified CVH metrics score and change in cognitive functions 2 decades later in patients with pre-existing coronary artery disease. A subset of 200 men (mean age at baseline 57.3 ± 6.3 years) who previously participated in a secondary prevention trial (1990 to 1997) underwent cognitive evaluation 14.6 ± 1.9 years after baseline (mean age 72.3 ± 6.2 years, T1 evaluation), and were re-evaluated for cognitive performance 19.9 ± 1.0 years after baseline (mean age 77.2 ± 6.4 years, T2 evaluation). A CVH metrics score at baseline was calculated, including 3 health parameters and 4 health behaviors. We have scored each of these CVH metrics into best (2 points), intermediate (1 point), and poor (0 points) levels. Cognitive function was assessed using the NeuroTrax Computerized Battery. A linear mixed model was used to assess change in cognitive functions between T1 and T2 cognitive evaluations. Among the 200 patients, 68 (34.0 %) had ≤7 (bottom group), 85 (42.5%) had 8 to 9 (middle group), and 47 (23.5%) had ≥10 (top group) CVH metrics points. After adjustments, the top group of CVH score versus others was associated with slower decline in the overall cognitive performance composite z-score (0.23 ± 0.09, p = 0.009) and on tests of executive and visual spatial functions (0.23 ± 0.11, p = 0.047, and 0.49 ± 0.17, p = 0.004, respectively). In conclusion, an inverse association was observed between the score of best CVH metrics and cognitive decline. Lifestyle factors are important predictors of late-life decline in cognitive function among high-risk patients. © 2017 Elsevier Inc. All rights reserved. **(Am J Cardiol 2017;■■:■■–■■)**

Many vascular risk factors are shared predictors for poor brain health and have been found to be associated with cognitive impairment and dementia.[1,2] In 2010, the American Heart Association introduced a metric defining the concept of ideal cardiovascular health (CVH) metrics for the healthy general population.[3] Several studies have demonstrated that a higher number of ideal CVH metrics were associated with a lower rate of cardiovascular events,[4] stroke,[5] and all-cause mortality.[4,6,7] The CVH score was shown to be linked to lower risk of cognitive impairment and dementia.[8–10] However, little is known about the collective association between CVH metrics and cognitive decline among patients with pre-existing coronary artery disease (CAD), which are characterized by their high-vascular risk profile and have a high risk of cognitive impairment.[11,12] Furthermore, most studies[13–15] estimated cognitive function at only a single time and therefore were unable to determine whether ideal CVH is associated with cognitive decline. We based our study on components of the CVH metrics, yet with modifications to adjust the tool to patients with pre-existing CAD.[11] We investigated the association between the modified CVH metrics score and change in cognitive functions 2 decades later in patients with pre-existing CAD.

Methods

The sample for the present study includes participants who previously participated in the Bezafibrate Infarction Prevention (BIP)[16] study, a large multicenter, placebo-controlled randomized clinical trial that has investigated the efficacy of bezafibrate 400 mg daily in secondary prevention among participants with established stable CAD[16,17] who are participating in the BIP Neurocognitive study. Patients included in the BIP Neurocognitive Study (mean age at baseline 57.3 ± 6.3 years) were recruited from 8 medical centers located at the center of Israel, have completed a diary food evaluation (48% of a total of 1,232), and have undergone 2 follow-up evaluations. The first follow-up evaluation (T1, n = 558; 308 of the patients had complete cognitive and CVH metrics measurements; mean age 72.3 ± 6.2 years) was performed during 2004 to 2008, an average of 15.0 ± 3.0 years after recruitment, assessing neurovascular and cognitive functions. Patients were reassessed for cognitive function 19.9 ± 1.0 years after recruitment during 2011 to 2013 (T2, n = 351; 200 of the patients

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The work was performed at the Department of Neurology and Joseph Sagol Neuroscience Center, Chaim Sheba Medical Center, Israel.

See page •• for disclosure information.

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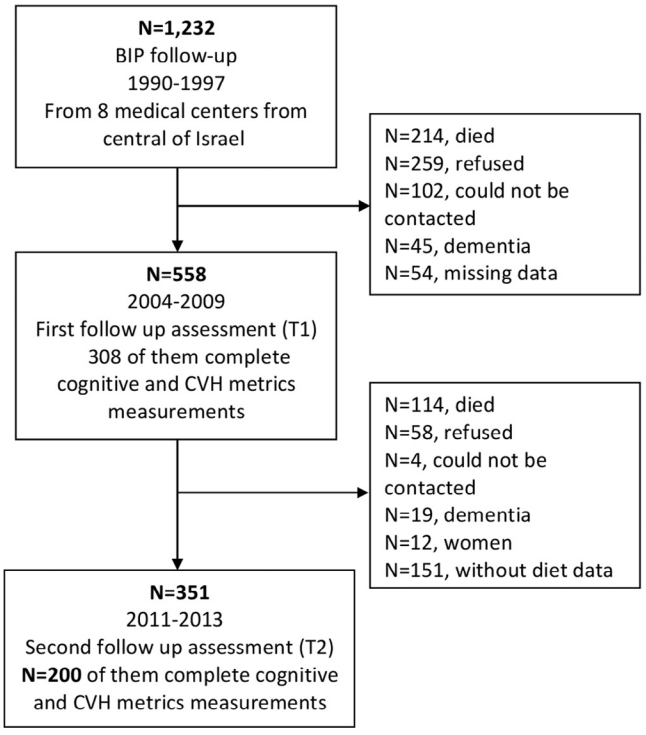

Figure 1. Study flowchart of the cohort.

had complete cognitive and CVH metrics measurements; mean age 77.2 ± 6.4 years). The mean time interval between the 2 cognitive assessments was 4.8 ± 1.3 years. A study flowchart is depicted in Figure 1. The 2 late-life evaluations took place at a central research center (the Sagol Neuroscience Center) or, if unable or unwilling to attend the medical center, were assessed at their residence. The study was approved by the local institutional review board and informed consent was obtained from all patients.

We have measured the following 3 health factors (fasting plasma glucose, low-density lipoprotein cholesterol, blood-pressure) and 4 health behaviors (smoking, obesity, physical-activity and adherence to Mediterranean diet). We have scored each of these CVH metrics into best (2 points), intermediate (1 point), and poor levels (0 points) (Supplementary Table S1). The health factors were (1) low-density lipoprotein cholesterol defined as best (160 mg/dl); and (2) BP—measured after rest in a seated position by experienced research nurses using a manual mercury sphygmomanometer. The average of the 2 measurements was used to classify BP status as best (systolic blood pressure [SBP] 140 and DBP >90 mm Hg). We have not considered BP therapy because all our patients had CAD. (3) fasting plasma glucose was defined as: best (/dL) and poor >125 mg/dL). The health behaviors included (1) smoking—participants were classified as "never," "former," or "current" smokers from self-reported information; (2) body mass index (BMI)—height and weight were measured at baseline without shoes using a standard stadiometer and an electronic weighing scale; BMI was classified as best (<25 kg/m^2), intermediate (25 to 30 kg/m^2), or poor (>30 kg/m^2); (3) physical activity—assessed by asking participants, "Do you participate in one or more of the following activities such as walking, swimming, jogging, gymnastics, biking, dancing, tennis, gardening, gym and rehabilitation activities?" and "How many times per week do you engage in physical activity?" Walking, swimming, gymnastics, biking, dancing, tennis, gardening, and rehabilitation activities were categorized as moderate intensity and jogging and gym as vigorous intensity. Participant responses were categorized as best (≥150 min/week moderate or vigorous intensity, or 75 min/week vigorous intensity), intermediate (1 to 149 min/week moderate or vigorous intensity, or 1 to 74 min/week vigorous intensity), and poor (none). (4) Diet, or adherence to a Mediterranean diet,[18] was evaluated from a self-administered 4-day diary record to evaluate detailed information of consumption of specific groups of foods: (1) vegetables, (2) fruits and nuts, (3) fish, (4) olive oil and monounsaturated fat, (5) fiber-rich whole grains, (6) legumes, (7) alcohol consumption, (8) fatty meat, and (9) cheeses. For each group, the median consumption for male gender was calculated. One point was given for patients with higher than the median consumption of food groups 1 to 6, whereas 0 point was given for lower than the median consumption. For alcohol consumption, 1 point was given for the recommended alcohol consumption of 5 to 25 g/day for women, and 10 to 50 g/day for men. For higher or lower alcohol intake, 0 was given. Groups 8 and 9 are known as harmful according to the principles of the Mediterranean diet. Patients with higher than the median consumption received 0, and for lower consumption, 1 point was given. For each patient, the total points of adherence were calculated. Patients with >5 points were categorized into the best group, 4 to 5 into the intermediate group, and <4 into the poor group of adherence to Mediterranean diet.

Methods for assessment of vascular risk factors at baseline of the BIP study are described elsewhere.[19] Blood samples were drawn from each study participant at baseline of the BIP trial (1990 to 1992), before randomization. Education, occupation, and place of birth, important indicators of socioeconomic status, were assessed through a baseline questionnaire. We included data on birthplace, which is an important key indicator of socioeconomic status disparities and, possibly, of genetic predisposition. In addition, previous studies suggest that risk of cognitive impairment differs between Israeli-born and immigrant populations.[20,21]

Participants completed a computerized cognitive testing (NeuroTrax Corporation, Bellaire, TX). A description of the tests included has been published elsewhere.[22] The psychometric properties of the tests exploit the advantages of computerized testing, providing precise accuracy and reaction time measurements. The tests are interactive and adaptive, adjusting the level of difficulty depending upon performance. The NeuroTrax software calculates raw composite scores for each cognitive domain, namely, memory, executive function, visual spatial processing, and attention. In addition, a composite score was computed as a weighted average of all summary scores from each domain.

Dementia and incident stroke during follow-up were determined by an adjudication committee composed of 3 investigators, 2 of which were experienced board-certified neurologists. Dementia was determined based on the sum of cognitive evaluation, clinical interview, and data collected, and in accordance with the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria.[23] Stroke was defined according to World Health Organization criteria.[24]